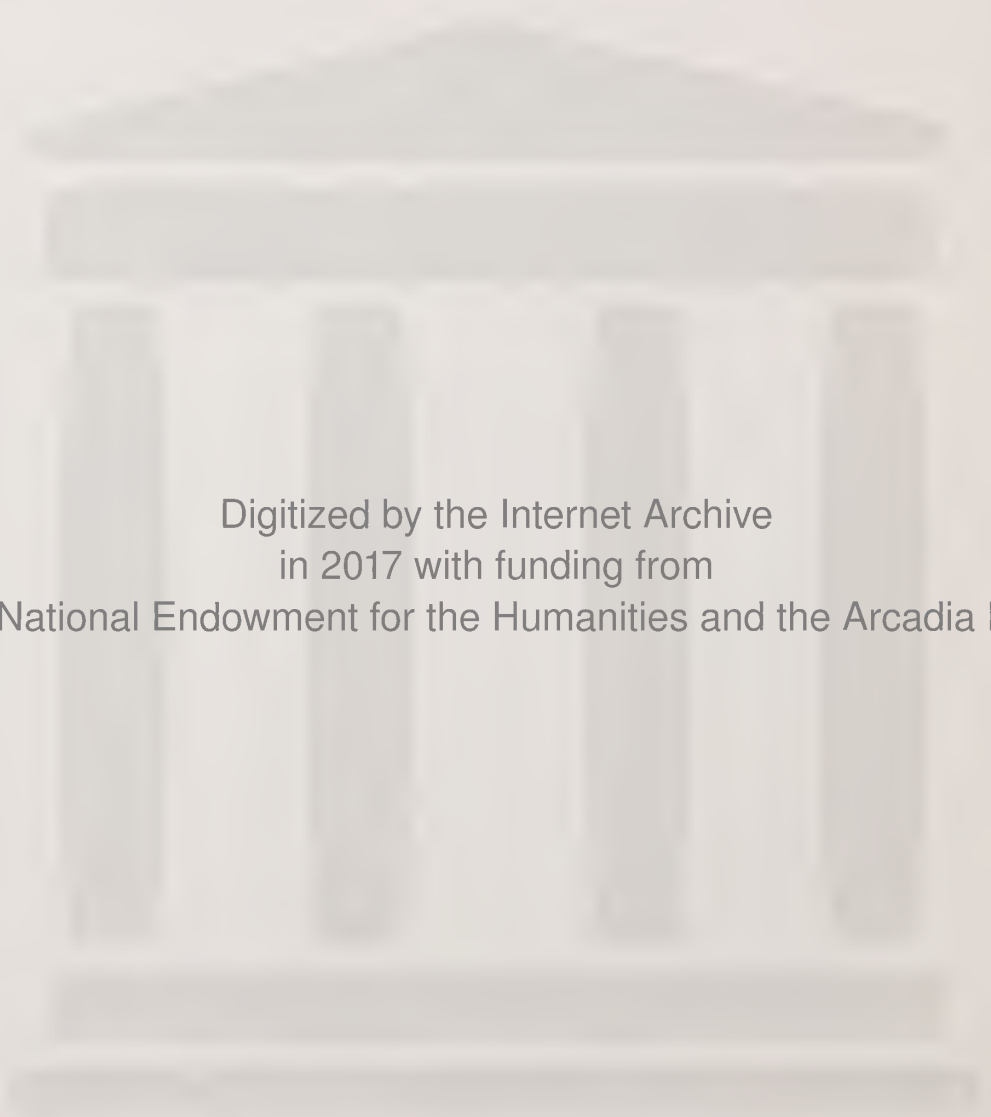




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# BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

## C O N T E N I D O

INSULIN AND GLUCOSE HOMEOSTASIS IN THE EARLY PERIOD  
AFTER ISLET CELL TRANSPLANTATION

*DIPYLIDIUM CANINUM* IN PUERTO RICO:  
REPORT OF A HUMAN CASE

THE INFLUENCE OF BLOOD TRANSFUSIONS ON  
KIDNEY TRANSPLANT SURVIVAL

EDITORIAL: ISLET CELL TRANSPLANTATION

CARTA AL EDITOR

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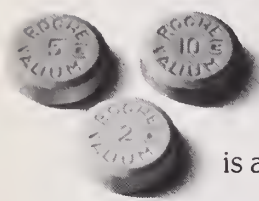
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VOL. 71

NUM. 7

JULIO 1979

# A character all its own.



Valium (diazepam/Roche) is a benzodiazepine with a character all its own.

Pharmacologically, it is a potent skeletal muscle relaxant and anticonvulsant (in adjunctive use), as well as an antianxiety agent. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

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**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

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Final classification of the less-than-effective indications requires further investigation.

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds, lesions of the eye, tuberculosis of the skin; most viral skin lesions (including herpes simplex, vaccinia, varicella).

### WARNINGS

*This product is not for ophthalmic use.*

In the presence of systemic infections, appropriate systemic antibiotics should be used

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Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant women has not been absolutely established. In laboratory animals, increases in incidence of fetal abnormalities have been associated with exposure of gestating females to topical corticosteroids in some cases at rather low dosage levels. Therefore, drugs of this class should not be used extensively on pregnant patients in large amounts or for prolonged periods of time

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May prove irritating to sensitized skin in rare cases. If irritation occurs, discontinue therapy. Staining may occur.

Signs and symptoms of systemic toxicity: electrolyte imbalance, or adrenal suppression have not been reported with Vioform-Hydrocortisone. Nevertheless, the possibility of suppression of the pituitary-adrenal axis during therapy should be kept in mind, especially when the drug is used under occlusive dressings, for a prolonged period, or for treating extensive cutaneous areas since significant absorption of corticosteroid may occur under these conditions, particularly in children and infants.

Vioform may be absorbed through the skin and interfere with thyroid function tests. If such tests are contemplated, wait at least one month between discontinuation of therapy and performance of these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine. Prolonged use may result in overgrowth of non-susceptible organisms requiring appropriate therapy.

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*Ointment*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base, tubes of 20 Gm.

*Lotion*, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben and perfume Flora in water, plastic squeeze bottles of 15 ml.

*Mild Cream*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water, tubes of 1/2 and 1 ounce.

*Mild Ointment*, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base, tubes of 1 ounce.

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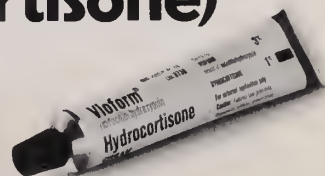
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## ASOCIACION MEDICA DE PUERTO RICO

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I N D I C E

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- \* **Insulin and Glucose Homeostasis in the Early Period After Islet Cell Transplantation** ..... 254  
*Luis H. Toledo-Pereyra, MD, PhD, Patricia Cromwell, BS, Steven E. Malcom, MS and José Goldman, MD*

In this issue of the Bulletin, Toledo-Pereyra, et al, describe the blood glucose and plasma insulin response immediately after adult islet cell transplantation in rats. According to their results the early glucose drop and serum insulin increase represent the sequential action first of the insulin present in the islet cell preparation just transplanted, thereafter, the insulin released by damaged islets during transplantation and several days later the insulin secreted by the transplanted cells.

In an editorial review published with this article, Aguiló presents the current state of the art regarding islet cell transplantation.

- \* **Dipylidium Caninum in Puerto Rico: Report of a Human Case** ..... 258  
*Mark W. Oberle, MD, Wilda B. Knight, MS and Luisa Hernández, MT*

Although several hundred cases of human dipylidiasis have been reported in the world literature, only one case has been previously described in Puerto Rico. In this issue, Oberle et al present the clinical features and therapeutic approach used to control an infection with *D. caninum* in a 20-month female patient. The authors present a brief discussion of the drugs currently available to treat this infection.

- \* **The Influence of Blood Transfusions on Kidney Transplant Survival** ..... 261  
*J. A. Ramírez Sánchez, MD and E. A. Santiago Delpín, MD, FACS*

In this article, the authors attempt to summarize the published data regarding the effects of blood transfusion on the survival of patients receiving kidney transplant. The authors emphasized not only the beneficial effects of blood transfusions, but also the number and the timing of blood transfusions necessary to achieve these beneficial effects. At a time when the number and survival of patients with end stage renal disease appears to be increasing and considering that renal transplantation has become widely accepted in the treatment of end-stage renal disease, this article presents pertinent information to all of our readers involved in the medical care of this group of patients.

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*Francisco Aguiló, Jr., MD, FACP*

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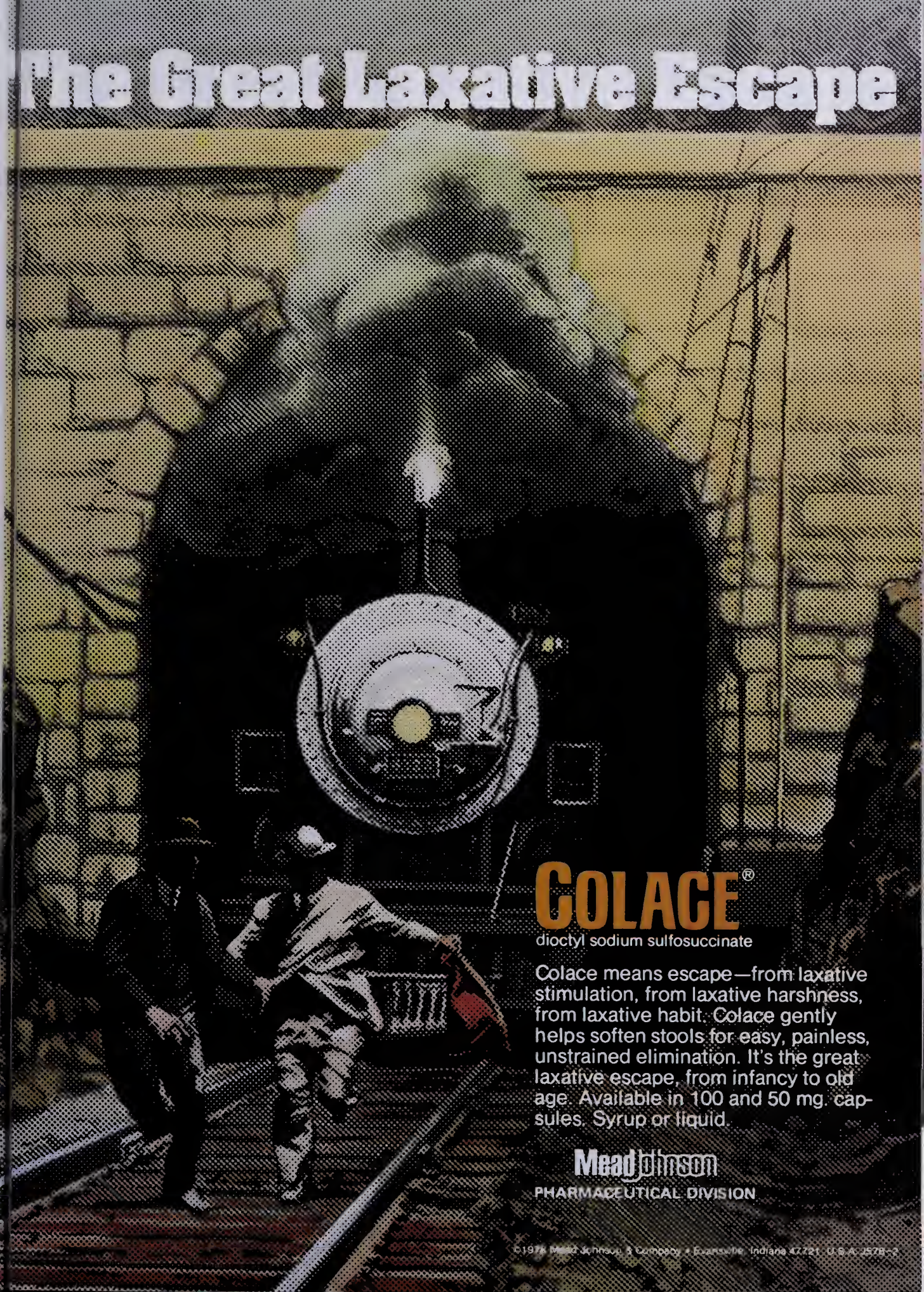
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**\*Indications:** Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, the FDA has classified the indications as follows:

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1. For the relief of symptoms associated with cerebral vascular insufficiency.
2. In peripheral vascular disease of arteriosclerosis obliterans, thromboangiitis obliterans (Buerger's Disease) and Raynaud's disease.

Final classification of the less-than-effective indications requires further investigation.

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Parenteral administration is not recommended in the presence of hypotension or tachycardia.

Intravenous administration should not be given because of increased likelihood of side effects.

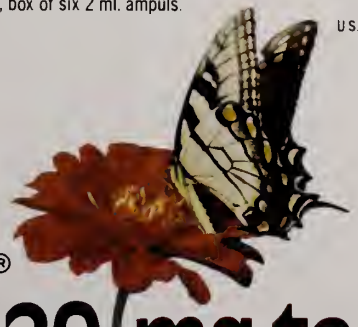
**Adverse Reactions:** On rare occasions oral administration of the drug has been associated in time with the occurrence of hypotension, tachycardia, nausea, vomiting, dizziness, abdominal distress, and severe rash. If rash appears the drug should be discontinued.

Although available evidence suggests a temporal association of these reactions with isoxsuprine, a causal relationship can be neither confirmed nor refuted.

Administration of single dose of 10 mg. intramuscularly may result in hypotension and tachycardia. These symptoms are more pronounced in higher doses. For these reasons single intramuscular doses exceeding 10 mg. are not recommended. Repeated administration of 5 to 10 mg. intramuscularly at suitable intervals may be employed.

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**Precautions:** Use with caution in patients with cardiac disease, hepatic or renal impairment. Concurrent administration with certain antibiotics, i.e., clindamycin, erythromycin, troleandomycin, may result in higher serum levels of theophylline. Plasma prothrombin and factor V may increase, but any clinical effect is likely to be small. Metabolites of guaifenesin may contribute to increased urinary 5-hydroxyindoleacetic acid readings, when determined with nitrosonaphthol reagent. Safe use in pregnancy has not been established. Use in case of pregnancy only when clearly needed.

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# INSULIN AND GLUCOSE HOMEOSTASIS IN THE EARLY PERIOD AFTER ISLET CELL TRANSPLANTATION

Luis H. Toledo-Pereyra, MD, PhD, Patricia Cromwell, BS  
Steven E. Malcom, MS and José Goldman, MD

**Summary:** This study attempts to define the kinetics of plasma glucose and serum insulin after adult islet cell transplantation in rats every two hours for 24 hours and then daily for one week. A sharp decrease of plasma glucose was noted in the first 4-6 hours after transplantation, which occurred concurrently with a sharp increase in serum insulin levels. Consequently, a return to normal levels was noted after two days of hypoglycemia. These studies are of some help in the understanding of the physiology of the transplanted islet cells.

**Resumen:** Este trabajo analiza la respuesta de la glucosa sanguínea e insulina sérica cada dos horas por el primer día y después cada día por una semana de los islotes pancreáticos transplantados en ratas tratadas con streptozotocina. La glucosa sanguínea descendió rápidamente cuatro a seis horas después del trasplante. Esta respuesta ocurrió al mismo tiempo en que los niveles de insulina sérica aumentaron. Posteriormente estos valores regresaron a los niveles normales después de dos días con niveles altos de glucosa sanguínea. Estos resultados

permiten un mejor entendimiento de la fisiología de los islotes pancreáticos transplantados.

An initial normoglycemic response is routinely observed in the first day after islet cell transplantation, followed by a hyperglycemic condition in the subsequent two to three days, with a further return to normoglycemic levels thereafter. The theoretical implications related to this glycemic response have been mainly associated with release of insulin by damaged islets (2), or with graft rejection in the allotransplant model (5). Recently, Matas and his associates (2) demonstrated that these glycemic changes following neonatal islet cell transplantation were probably due to release of insulin from damaged islet cells rather than graft acceptance. We have carried out further these observations by studying the blood glucose and plasma insulin response every two hours after adult islet cell transplantation in rats for the first 24 hours, and then daily thereafter for the subsequent three weeks.

## Materials and Methods

---

*From the Department of Surgery, Section of Transplantation and Surgical Research and the Department of Medicine, Section of Endocrinology Research, Henry Ford Hospital, Detroit, Michigan.*

*This work was supported by a Henry Ford Hospital Institutional Grant (730-0786) from Ford Foundation.*

*Address reprint requests to: Dr. Toledo-Pereyra, Department of Surgery, Section of Transplantation and Surgical Research, Henry Ford Hospital, 2799 West Grand Boulevard, Detroit, Michigan 48202.*

Pancreases obtained from adult male Lewis rats were minced into 1-2-mm pieces, the pancreatic tissue was dissociated with 8.0 mg of collagenase (Worthington type IV, lot No. 48K186, 190 U/mg) per pancreas. After dissociation, the tissue was separated by the Ficoll gradient separation technique (1). Islets were recovered and counted under the microscope

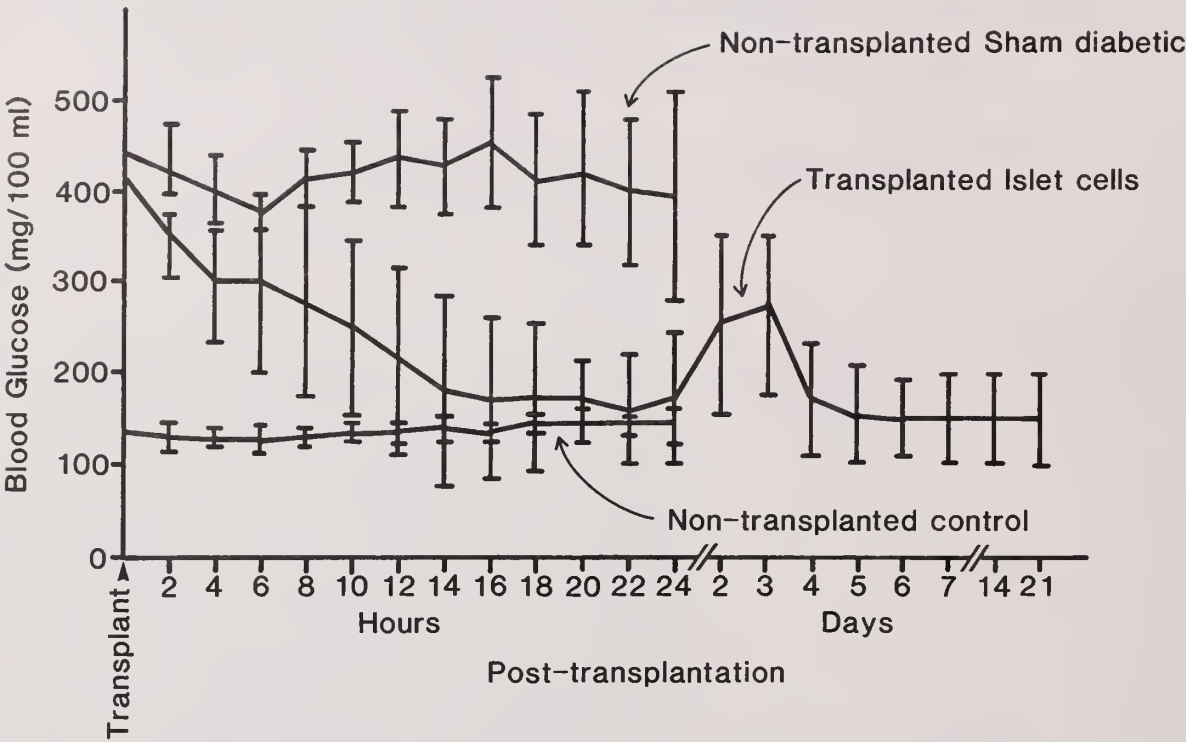


Figure 1: Plasma glucose levels ( $M \pm SD$ ) in the normal control, sham-operated diabetics, and the islet cell transplant groups.

prior to transplantation. Islet cells obtained from six donors in a range of 950-1140 were transplanted into the portal vein of recipient animals previously made diabetics by streptozotocin treatment (65 mg/Kg) (Upjohn Company). Transplantation was performed several weeks after the levels of glycemia were equal to or more than 400 mg/dl. Immediately after transplantation, blood samples were obtained for plasma glucose (6) and serum insulin (4) measurements, which were made every two hours for the first 24 hours, then every day for the first week and then twice a week for at least the following two months.

Three groups of animals were studied. Group I ( $n=6$ ) was the normal control that received no transplantation and was not diabetic; group II ( $n=6$ ) a sham-operated diabetic group of animals, and group III ( $n=6$ ) was the recipient animals that received islet cell transplantation in the way outlined above. The statistical

analysis was obtained by utilizing the Student's  $t$  test and the analysis of variance method.

Results

Figures 1 and 2 show the plasma glucose and serum immunoreactive insulin levels for all groups. All normal controls without an islet cell transplant had random plasma glucose levels below 150 mg percent. The levels of serum insulin in the control animals were high in the first four hours after transplantation with a decrease in the next four hours and a subsequent raise at 20 hours. The sham-operated rats that received no islet cell transplant showed high levels of blood glucose ( $\geq 400$  mg/dl) at all



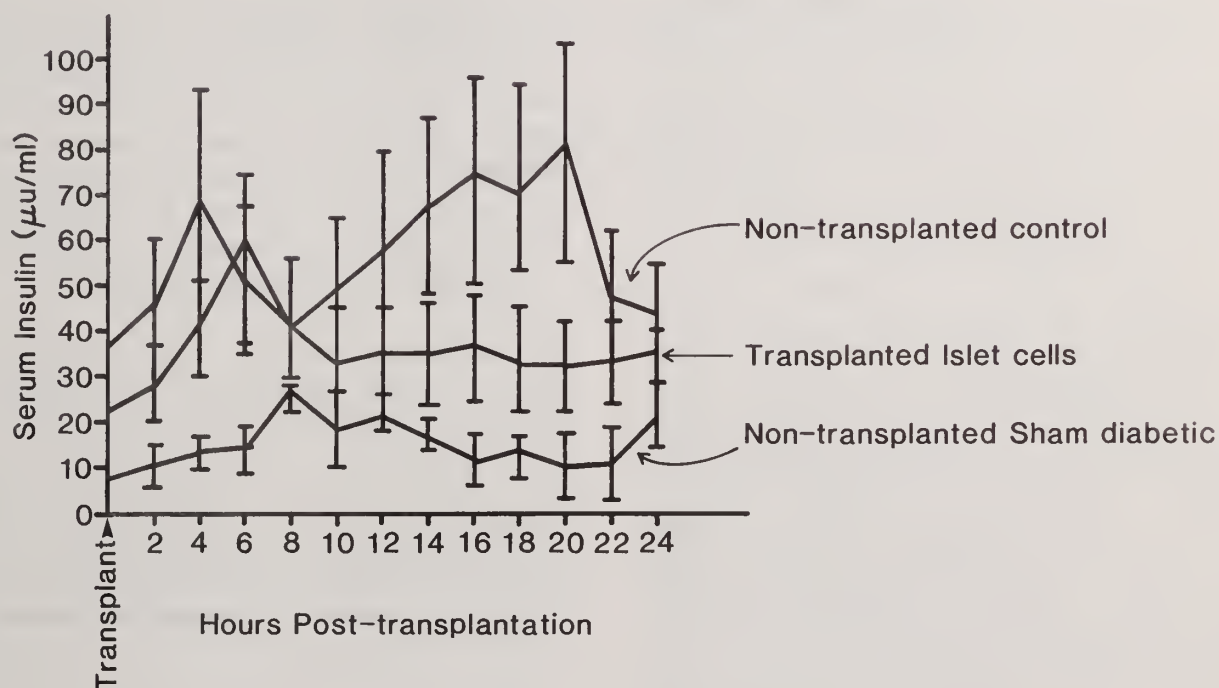


Figure 2: Serum insulin levels ( $M \pm SD$ ) in the normal control, sham-operated diabetic, and the islet cell transplant group.

times with uniformly low levels of serum insulin. The islet cell transplanted group showed a sharp decrease of plasma glucose in the first 4-6 hours after transplantation which occurred concurrently with a sharp increase in serum insulin levels; subsequently, there was a slow decline of plasma glucose, as well as of serum insulin values. The lowest values of plasma glucose and serum insulin were observed at 24 hours after transplantation. A subsequent increase in plasma glucose was observed during days 2 and 3 posttransplantation with a subsequent return to normoglycemia.

### Discussion

Our data suggest that the initial drop in

plasma glucose during the first few hours after transplantation is due to insulin that is already in the medium of the islet cell preparation that is being injected. The second drop in blood sugar observed from six to twenty-four hours post transplantation is most probably due to insulin released from damaged islets. Then, the newly transplanted islets do not start functioning until two to three days later in which the plasma glucose returns to normal values.

When explaining these findings, it should be taken into consideration that the half life of insulin (human) is around 3-5 minutes; therefore, 50 percent of the insulin already present in the islet cell preparation will be utilized in the first five minutes and only 1 percent of that insulin will be eliminated in approximately 30

minutes. It is also possible that the hyperglycemia present in the diabetic rats may stimulate the secretion of insulin by newly transplanted islets. Nevertheless, with the information currently available we can indicate that the pattern of plasma glucose most probably represents the sequential action first of the insulin present in the initial islet cell preparation, thereafter, the insulin released by damaged islets and several days later, the insulin secreted by the transplanted islet cells.

It appears evident that islet cell destruction occurs in the process of collagenase digestion. This has been demonstrated by Matas and his associates (2, 3) and also confirmed in our own experiments. Collagenase treatment is an aggressive, potentially harmful but the only available method for islet cell separation which gives adequate results at the present time. Needless to say that the inconsistency of collagenase is noteworthy and better methods should be worked out for islet cell separation (7).

It is remarkable to see that the early observations in islet cell allografts in the first day after transplantation were attributed to immunological changes rather than physiological readjustments. Our studies are in agreement with other researchers (2) in that the immediate sharp drop of blood sugar observed after trans-

plantation should not be taken into consideration for final acceptance of normoglycemia, but rather subsequent values 2-3 days thereafter should only be considered. This kinetic response of plasma glucose and serum insulin observed in hourly basis immediately after transplantation should be of some help in understanding the physiological and immunological responses of transplanted islets.

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## DIPYLIDIUM CANINUM IN PUERTO RICO: REPORT OF A HUMAN CASE

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**Summary:** *Dipylidium caninum* infection was documented in a 20-month-old girl who had a prolonged history of anal pruritis and mild anorexia. Two attempts at treatment with paromomycin failed, but a single dose of niclosamide produced a clinical and parasitologic cure. This is the second confirmed case of human dipylidiasis reported from Puerto Rico.

**Resumen:** Infección con *Dipylidium caninum* fue documentada en una niña de 20 meses con historial de pruritis y anorexia benigna. El tratamiento con paromycina falló en dos ocasiones, sin embargo, una sola dosis de nicloslamide produjo curación clínica y parasitológica. Este es el segundo caso confirmado de dipylidiasis humano reportado en Puerto Rico.

*Dipylidium caninum* is an uncommon

cestode parasite of humans. The adult tapeworm normally inhabits the upper small intestine of dogs or cats. The mature proglottides move actively through the host's anal sphincter where they disintegrate. The egg capsules are then consumed by larvae of various fleas (*Ctenocephalides*, *Pulex*) or the dog louse (*Trichodectes canis*). Dogs, cats, and occasionally humans are infected after ingesting fleas or lice containing the cysticercoid form of the parasite.

Several hundred cases of human dipylidiasis have been reported (1-5). In Puerto Rico the first human case was reported by Hoffman in 1926 (6). We describe here another confirmed case, along with some therapeutic observations.

### Case Report

In May 1976, a 20-month-old girl from Naranjito was referred for refractory parasitosis to Dr. Pedro Flores-García at the Bayamón Regional Hospital. The mother had noted parasites in the child's stool for the previous half year. Anal pruritis and mild anorexia were reported. Defecation was said to have been sporadic with occasional blood and mucous. The child had had brief contact with a neighbor's dog.

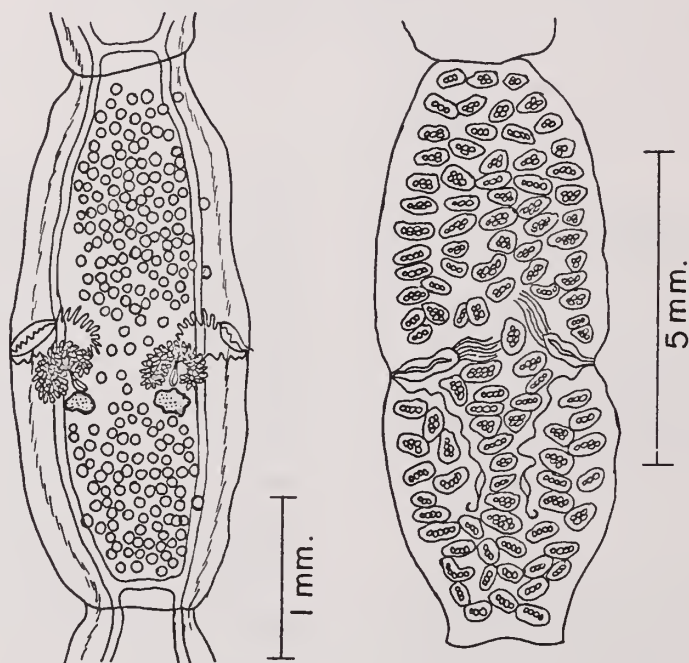
The physical examination was unremarkable. The weight was 11.6 kilograms (between 10th and 25th percentile), hematocrit 37 percent, white blood cell count 8,000/mm<sup>3</sup> with 23 percent polymorphonuclear cells, 76 percent lymphocytes, and 1 percent eosinophils. The stool was grossly normal, but ery-

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# Dipylidium caninum



Mature proglottid

Ripe proglottid  
filled with egg  
balls

throcytes and white blood cells were detected by microscopic examination. The clinical laboratory at the Bayamón Regional Hospital detected numerous proglottides of *Dipylidium caninum*. The San Juan Laboratories of the Center for Disease Control (CDC) confirmed this observation.

The patient was given 50 mg/kg of paromomycin (Humatin\*) p.o. in four divided doses. However,

follow-up stool examination was still positive, and the mother noted "worms" in the anogenital area. A second course of paromomycin was attempted: 11 mg/kg t.i.d. for seven days. Parasitosis persisted. Finally niclosamide (Yomesan\*), 1 g in a single oral dose was prescribed. The patient accepted approximately half of the medication, but refused to take the full dose. Follow-up stool examination 7 days later was

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\* - Use of trade names is for identification only and does not constitute endorsement by the U. S. Public Health Service or the Department of Health, Education, and Welfare.

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negative. The patient failed to return for a 3-month follow-up examination, but the mother reported no symptoms at that time.

### Discussion

This case was typical of human dipylidiasis. The patient was young, had a history of contact with a dog, and experienced only mild symptoms — anal pruritis and mild anorexia. However, the mother was quite distressed by the persistence of the parasite, especially when she discovered motile “worms” near the child’s anus and labia. The report of occasional blood-streaked stools was not confirmed. A review of the literature showed one previous case of human dipylidiasis reported in Puerto Rico (6). Additional human cases have been suspected previously but never documented. However, the rarity of reports and the non-specific symptomatology concur in reducing the clinicians’ index of suspicion (4). Since the proglottides deteriorate quickly outside the intestinal tract, a stool examination might be reported as negative unless the specimen is fresh or preserved. The parasite can also be identified by the adhesive-tape method familiar from pinworm diagnosis (4). On microscopic examination, the mature proglottides of *Dipylidium caninum* are vase-shaped, with two lateral genital pores (Figure 1). The proglottides contain numerous encapsulated egg clusters.

Niclosamide has replaced quinacrine (Atabrine\*) as the first choice drug for *Dipylidium caninum* and most other cestode infections (7). It is an Investigational New Drug (IND) and currently is available in the United States only through the Parasitic Disease Drug Service of

the CDC. Ordinarily niclosamide is not given to children under the age of 24 months, because it has not been studied sufficiently in this age group. Thus, paromomycin, the second choice drug for most cestodes (7) was prescribed initially. However, the infection persisted. Although the child accepted less than the full recommended dose of niclosamide, the prolonged illness terminated immediately after administration.

Niclosamide, as well as other drugs for uncommon or imported parasitoses, is readily available to physicians through the Parasitic Disease Drug Service. In Puerto Rico, these drugs can be obtained through the Department of Health, Communicable Disease Control Program, Division of Preventive Medicine (767-9122), or directly from the Parasitic Disease Drug Service Center for Disease Control, Atlanta, Georgia 30333 (404-329-3670).

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# THE INFLUENCE OF BLOOD TRANSFUSIONS ON KIDNEY TRANSPLANT SURVIVAL

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**Summary:** Blood transfusions induce the formation of antibodies. Because of this, transfusions have been traditionally withheld from transplant candidates. However, critical examination of human and animal data has surprisingly shown that transfused recipients have better chances of kidney survival than non-transfused recipients. Most studies show a beneficial effect and the evidence is very strong. The mechanism of this effect is unknown but it is currently thought that a form of active immunological enhancement may be operative. Appropriate measures to avoid risks and complications should be taken, and all candidates for cadaver kidney transplantation should receive blood transfusions before transplantation.

**Resumen:** La transfusión de sangre induce la formación de anticuerpos. Por esta razón, no se suelen transfundir los candidatos para trasplante. Sin embargo, al examinar los resultados de estudios clínicos y en animales, se llegó a la sorprendente conclusión que el recipiente de un riñón tiene mejores oportunidades de éxito si ha recibido transfusiones previas, que si no las ha recibido. Los datos son consistentes entre sí, y la evidencia en apoyo de esta conclusión es fuerte. Aunque se desconoce el mecanismo, se cree

que este efecto es resultado de facilitación inmunológica activa. Utilizando todas las medidas de cuidado para evitar complicaciones y minimizar los riesgos, aquellos candidatos para recibir un riñón de cadaver deben recibir múltiples transfusiones de sangre antes del trasplante.

Renal transplantation has become widely accepted in the treatment of end-stage renal disease. Many immunological factors influence kidney transplant survival. Factors such as sex, age and race group of both donor and recipient, HLA-match, ABO group, preformed cytotoxic antibodies as an index of pre-sensitization, original disease, and length of time on hemodialysis until transplantation have all been subject of extensive study. A subject of controversy concerns the use of blood transfusions in the anephric patient awaiting transplantation.

The patient with end-stage renal disease almost universally suffers from severe anemia. In the early days of transplantation blood transfusions were frequently given in order to correct this problem. However, it very promptly became evident that patients receiving blood transfusions developed antibodies against one or more histocompatibility antigens. The significance of this finding was thought to be quite relevant, because the amount of antibody formed in this way, directly correlated with graft loss from hyperacute rejection. As a result of these preliminary observations, a dictum was quickly established in which blood

transfusions were considered to be sensitizing agents and therefore were a negative factor in transplant survival. It became a widespread practice in both America and Europe to use as few blood transfusions as possible, and even to consider kidney transplantation contraindicated in patients who had received multiple transfusions.

However, in 1973, Opelz, et al, critically examined the data of patients with blood transfusions and reported the surprising conclusion that blood transfusions had a beneficial effect on the outcome of transplantation (1). This study was followed by a more complete study (2), in which failure to improve transplant results in the last few years was directly attributable to the practice of withholding blood transfusions from patients. As expected, these reports were met with considerable skepticism, giving rise to an outcry of criticisms and immediately triggering a flurry of activity in both experimental and clinical areas. This activity gradually shed light on the problem in such a way that study after study, in both man and animal, have corroborated the initial impressions of Opelz and Terasaki. A significant body of evidence has accumulated in the last three or four years in such a way that the vast majority of investigators in the field agree that blood transfusions have a beneficial effect on transplantation.

This situation has raised a number of questions which are critical in the assessment and treatment of kidney transplant candidates, but unfortunately, it has still not reverted the previous practice of withholding blood transfusions. However, the majority of important centers will be hesitant to transplant a cadaver kidney if the recipient has not received blood transfusions previously. This change in attitude started in early 1975, and is expected to eventually become universal, the final weight being carried by the

recent work by Opelz and Terasaki (3) and by Salvatierra's group (4) late in 1978.

It is the purpose of this review to present and comment on the available literature regarding the benefits of blood transfusions, and at the same time to pose several questions, most still unanswered, regarding the mechanism of action of blood transfusions, as well as the clinical practical details in this type of voluntary presentitization. Some of the questions raised include, the number of blood transfusions necessary to achieve the beneficial effect; the proper timing and scheduling of transfusions necessary to achieve the beneficial effect; and finally, the possible immunological mechanisms involved.

### Are Blood Transfusions Really Beneficial?

Opelz' first report on the apparent induction of unresponsiveness to kidney grafts by blood transfusions opened new directions in transplantation. In 1974, Murray (5), in a study designed to determine important factors in cadaver-donor kidney transplantation, also found that previous transfusions had a positive effect. Festenstein et al (6) found this effect to be true in the first large series to be studied, comparing also the influence of HLA matching and blood transfusions on the outcome of 502 renal graft recipients.

The findings of Opelz and Terasaki (7) were confirmed by Polesky and McCullough (8) from Minnesota, and by Persijn and Van Hoof (9) from Holland.

The reader is here referred to Van Es and Balner's excellent critical summary (10) which illustrates the vigorous activity occurring in this area during 1977 and 1978. Several additional studies both in humans and animals corroborated previous findings. Some investigators attempted to define the effect of specific blood preparations (11); others tried to



correlate the effect to prolonged uremia (12); one study was restricted to male patients (13). Studies done in mongrel dogs (14) and Rhesus monkeys (15) were all in keeping with previous findings. Another study considered the influence of center variation and presensitization (16). It appears that virtually all human and animal studies show the same result; blood transfusions improve graft survival; a few studies show no difference in graft survival; and none of the studies so far show any worsening of graft survival.

There is no proven correlation of transfusions to age, sex or race group, and the data are variable and conflicting (17). While previous pregnancy in itself improves graft survival (18), further improvement by transfusion was not shown. Neither the degree of uremia prior to transplantation, nor the original disease appear to have a special relationship to transfusions. Blood transfusion effect appears to be greater in bilateral nephrectomized patients. This effect could be due to a greater number of transfusions, rather than the effect of nephrectomy itself.

#### Number of Blood Transfusions Necessary to Achieve Optimum Effect

A study of 1,360 cadaveric renal transplant recipients from the U. C. L.A. transplant registry clearly demonstrated that transplant success rates increase in proportion to the number of transfusions given before operation (3). This study had a follow-up of four years, through which the positive correlation was maintained. No statistically significant effect of a single transfusion was found, contrary to other studies in humans (19) and in monkeys (20). Neither was a positive effect found if transfusions were given during the transplant operation as found by Freeman et al at Iowa (21) or by Stiller (22).

This finding has relevance in both planning presensitization and scheduling the blood transfusions. Furthermore it shed doubt on the theory (to be discussed below) that blood acts by preselecting or "weeding out" a high responding population. The fact that there is a direct correlation between number of blood transfusions and final outcome, favors the concept that this is an active immunological phenomenon. It was noted elsewhere that there is a greater frequency of antibody formation as more units are transfused.

Since there are no guidelines at present on how to decide on the exact number of blood transfusions, a number of centers are acting on the basis of Opelz data, that is, that five blood transfusions significantly improve results. Our transplant center is giving 5 blood transfusions as a minimum requirement to place the patient on the computer waiting list, followed by additional blood transfusions every one to four months depending on patient needs. This protocol will undoubtedly change in the future as specific data become available.

#### Timing of Blood Transfusions

While Brynger (13) states that at least two transfusions should be given about one month prior to transplantation, other authors give them according to dialysis facilities and patient requirements. It has been suggested that waiting for longer periods between initial and final challenges may be beneficial (20, 23). This may be in consonance with data that relates better survival with prolonged hemodialysis, although these impure observations carry so many variables that it is impossible to identify time alone as the significant element.

Transplant and dialysis units will probably give transfusions according to their facilities, the availability of blood, and patient



requirements. Planned presensitization by some groups is being given as one or two weekly blood transfusions for a total of five, but there is no evidence whatsoever that this is an ideal scheduling of transfusions, and this may change in the future.

### Blood Preparations

Perkins (24) reports that processing for leukocyte-poor packed red blood cells leaves from 3 to 20 percent white blood cells in the preparation; up to  $100 \times 10^6$  WBC may be present in these fractions. Twelve to 35 percent of patients on "mixed" (whole blood and other fractions) blood administration develop significant titers of antibodies, while only 6 to 17 percent in WBC-poor preparations. The formation of antibodies is directly proportional to the number of units transfused and their leukocyte content. It is inferred from these results that it will be more difficult to find a negatively cross-matched donor kidney, although neoformation of cytotoxic antibodies does not mean non-transplantability; neither does it mean that the titers will not change with time. It is common to observe wide fluctuations in antibody titers both before and after transplantation.

Enhanced graft survival with frozen red blood cells was noted only by Fuller et al (11), while best results were observed with whole blood by Terasaki (2, 3). Data on this aspect is available only from small series of patients and results are variable, but frozen blood is presumably less antigenic and should not result in better graft survival.

### Hazards of Transfusion

Transmission of serum hepatitis is obviously of first concern and probably was

of paramount importance in withholding blood transfusions in the first place. However, with modern testing techniques (routine in all banks) and the decreasing practice of using paid donors, this hazard can be kept to a minimum. Unfortunately, present technology does not provide serologic marking for Non A, Non B hepatitis, and introduction of this disease in a dialysis unit may be catastrophic. However, whatever risk remains may be worth taking when it is considered that performing a cadaver transplant without previous transfusions is, in itself, a true high-risk procedure. A more insidious risk, perhaps more difficult to detect, is that of transmitting cytomegalovirus. This ubiquitous virus results in increased morbidity and mortality in immunodepressed hosts, specifically after bone marrow transplantation (25). No projections on the magnitude of this potential problem can be made at present.

The risk of presensitization is controversial. It is recognized that blood transfusions lead to the formation of lymphocytotoxic antibodies. Donors are eliminated if recipient serum reacts with donor lymphocytes (positive cross-match test). Also, broadly reactive antibodies against the majority (more than 50 percent) of a random panel of donor's lymphocytes (most use 15 random donors, we at our institution use 25) has been considered to be a poor prognostic sign for cadaveric transplantation. However, even this last point has been a topic for discussion since it has been reported that even patients with high percent of cytotoxic antibodies, if they find a suitable donor with a negative crossmatch, will not necessarily do worse (26). The most important factor appears to be a sensitive cross-match technique. However, there is still controversy in this area (27).

In general, the formation of antibodies is directly related to a number of transfusions and their white cells content. There are patients who respond with high titers of antibodies

after only a few transfusions. They are called "high responders". "Non-responders", those who continue with low titers even after a large number of transfusions, have the best prognosis. A study shows that presensitized patients, those with the most number of transfusions have the worst prognosis. But even this group is better off than those never transfused. Best prognosis is for those who fail to develop cytotoxic antibodies in spite of multiple transfusions.

Caution, nevertheless, is in order. Blood is a biological product with immensely valuable properties, even (as we have seen) in the transplant field. However, it has attendant risks and complications and we must guard against its indiscriminate use. Appropriate measures and safeguards against infections and reactions, and monitoring and watchfulness are required now as always, lest inappropriate use lead to diminution of its beneficial properties.

### Blood Transfusions in Recipients of Familial Kidneys

Improvement of results has been found even in living related donor transplantation (28). Other series addressing this point do not report worsened survival or presensitization. However, we are still reluctant to use blood in potential recipients of live related donors since the risk of presensitizing against that particular donor would upset possible benefits from the blood transfusion. Experiments using third-party donors not sharing any HLA specificity with the future kidney donor will have to settle this issue.

### Possible Mechanisms for the Beneficial Effect of Transfusions

A variety of mechanisms have been pro-

posed to explain this rather surprising effect. First, a passive mechanism akin to that described in rodents has been proposed for humans. In some strains of mice, a high antibody titer response is seen after injection of synthetic polypeptides. Other animals in the same strain may respond with less vigor to the injection of the material. The latter are called "low responders", and the former, "high responders". It is not clear whether this artificial classification applies also the response on more complex antigens or antigen systems. The fact that two series have reported beneficial effects from a single blood transfusion could signify that one transfusion is preselecting a high responding, high risk population by virtue of the high response to the biological product. The theory would predict that this population would do very poorly with a kidney transplant. However, the fact that most series correlate the survival directly with the number of blood transfusions seems to militate against this theory as the only explanation.

A second mechanism is proposed in which an active immunological protection is afforded by the transfusion. One possibility is activation of suppressor T-cells which could decrease the immunological response. The formation of blocking antibodies (or blocking factors in general) that would lead to enhancement is another favored possibility. Similarly, the formation of anti-B-cell antibodies (anti-IA) could be operative also. Finally, the induction of specific unresponsiveness to major histocompatibility complex antigens of the graft by cross-reactivity of blood and kidney could also be operative. Still, in the final analysis, the critical question would still remain: what is the exact molecular basis for the development of cytotoxic sensitization on the one hand, and suppression of immunological activity on the other? Such an important point has relevance not only in the



transplant ambience but in cancer immunology as well. Once this positive effect of transfusions and graft survival is determined, a rational schedule for planned presensitization will be immediately available. In addition, these data will greatly enhance our understanding of this fascinating system in immunology, and its application to infection, transplantation, and cancer.

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## ISLET CELL TRANSPLANTATION

Although first attempted 17 years ago (1), pancreatic transplantation as a cure for diabetes mellitus has proceeded slowly. There have been practical lessons to be learned and innovative techniques to be mastered. Indeed, the problem has been redefined: at the end of this decade we are no longer after a "pancreatic transplant" but after an effective means of islet cell transplantation.

As in the "insulin story" of the 1920's, removing the ever-present exocrine component of pancreatic tissue called for ingenuity. This was provided by Lacy and Kostianovsky (2), who were able to disrupt the unwanted tissue cannulating and forcing fluid retrogradely into the pancreatic duct *in vivo*. This was complemented by digesting the minced tissue with collagenase, thus achieving dissociation of the islet cells from the exocrine component. The laborious task of separating the wanted cells was considerably aided by discontinuous density gradient separation techniques (3), which brought islet cells to the upper layers. Rodents were, and have remained, the usual experimental animals, especially rats and mice. By utilizing alloxan or streptozotocin, experimental diabetes can be reproducibly induced in these animals, and the effects of transplanted islets noted. This was originally done by Younoszai et al (4), utilizing intraperitoneal injections of islet cells. Consistent "cure of glucosuria, hyperglycemia, polyuria, polydipsia and weight loss were not lasting, however, until the portal route of transplantation was utilized. This was first shown by Kemp and co-workers in 1973, who found that among various routes tested, the portal vein gave the best results (5). This is probably due to the fact that this route provides almost immediate vascular supply to the transplanted islets and that such location is most physiologic, as normally, secreted insulin goes first to the liver. Under these circumstances, it appears that success is assured, provided enough islets are transfused. Morphologically, by 3 months post transplantation, well vascularized islets are seen juxtaposed to hepatocytes, without intervening endothelium (6).

Further progress was provided by Leonard and co-workers (7, 8). These investigators found that the neonatal pancreas could be easily dispersed through mincing and collagenase digestion and could be used without having to separate the exocrine pancreas. The success of such transplant is prompted by an 8-fold higher content of endocrine (relative to exocrine) tissue in neonatal pancreases.

In spite of not having reached its clinical goal, much progress has been made in clarifying the role played by the hyperglycemic milieu in the pathogenesis of chronic complications of diabetes, such as the thickening of the capillary basement membranes. Thus, Mauer and Sutherland (9-12) have clearly shown that post transplantation, the typical renal lesions previously produced in experimental diabetic rats, reverse or fail to progress. Similar data were found by Gray and Watkins (13). They could prevent such lesions appearing among rats that received curative islet transplants shortly after the induction of diabetes. Their diabetic rats also had typical retinal lesions, while the transplanted ones did not.

These findings have further encouraged clinicians and investigators alike to strive for the "perfect" control of the diabetic.

Much remains to be done before these animal experiments can be safely translated into humans. Even among rodents, allograft rejection is common, contrary to the uniform success of isologous islet tissue. Indeed, immunosuppressive regimens that are usually successful in preserving tissues such as kidney and heart across major histocompatibility barriers, have met with failure in the case of islet cell transplants. Care must also be exercised on the other hand, in preventing metabolic deterioration from the use of immunosuppressive agents. Sutherland and associates (14), for instance, found in islet transplanted dogs that prednisone was very diabetogenic. In fact, it was difficult for them to distinguish between the effects of rejection and the action of glucocorticoid!



In this number of the *Boletín*, Toledo-Pereyra and associates report their results and interpretation on the early findings in glucose and immunoreactive insulin levels upon adult islet cell transplantation in rats. In keeping with previous studies (6) they found that transplantation of islets through portal vein restores fasting plasma glucose levels to normal within 24 hours. Their original contribution addresses the question of how to explain the early glucose drop and serum insulin rise noted. A definitive interpretation would have required a more elaborate study. Yet their explanation seems to be a very plausible hypothesis: Preformed and released insulin could indeed account for the early insulin effect noted. Such studies should further clarify fundamental questions in relation to the physiology of transplanted islets cells.

In the meantime, one must strive to accomplish the best possible diabetic control in our patients. This should involve closer blood glucose monitoring by patients and physicians. The use of glycosylated hemoglobins (particularly Hb A<sub>1C</sub>) should be incorporated to our armamentarium. Therapeutic regimes should be similarly reviewed to include, if need be, 2 or 3 - even four - doses of insulin per day. This will require a lot of personal and group motivation for which the physician must feel primarily responsible. The availability of programmable "open loop" systems could afford a means to achieve such good control by means of frequent-even continuous, insulin administration.

For the time being, life for our insulin-dependent diabetics will not be any easier. Neither for us, in spite of our advancing knowledge and resources.

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## LA VACUNA DE NEUMOCOCOS EN LOS NIÑOS

José E. Sifontes, MD

Esta breve comunicación obedece a una encomienda de la Asociación Puertorriqueña del Pulmón al efecto de resumir las indicaciones para la vacuna de neumococos en los niños.

La vacuna consta de 14 tipos polisacáridos de neumococos y está aprobada para uso comercial desde febrero de 1978 (1). Las reacciones adversas informadas hasta ahora han sido irritación en el sitio de la inyección y fiebre. Estas son más severas cuando se repite la vacunación dentro de un período menor de 3 años o en las personas que han tenido infecciones recientes por neumococos.

Siegel y colaboradores de la Escuela de Medicina de Pittsburgh estudiaron los tipos de neumococos que le causaron infecciones a los niños admitidos al Hospital de Niños de Pittsburgh tales como meningitis, sepsis, pleuresía y pulmonía. Encontraron que el 86 por ciento de los neumococos eran de los tipos contra los cuales protege la vacuna de neumococo. El 45 por ciento de las infecciones causadas por los neumococos sucedió en niños con afecciones predisponentes (que podrían considerarse indicaciones para la vacuna) tales como leucemia, linfoma, cardiopatía congénita, síndrome de Down, hidrocefalia, esplenectomía, drepanocitosis y otras hemoglobinopatías (2).

J. O. Kleen, de Boston University, y E. A.

Mortimer, de Case Western Reserve University, recomiendan que la vacuna de neumococos debe emplearse en los niños mayores de dos años de edad que están en riesgo de contraer enfermedades severas o potencialmente fatales por neumococos (3). Por ejemplo, los que sufren de anemia drepanocítica (sickle cell anemia), los que han tenido una esplenectomía y los que tienen nefrosis lipoidea.

Griffin, de la Universidad de Tennessee, menciona entre las personas que se beneficiarían de la vacuna, todas aquellas de más de dos años de edad afectadas por enfermedades crónicas, diabetes mellitus y trastornos funcionales cardiorrespiratorios, hepáticos o renales (4).

Las indicaciones para la vacuna de neumococo en niños están en proceso de reevaluación. Se está valorando el significado clínico del descubrimiento de tipos de neumococos como el 6B resistentes a la penicilina y muchos otros antimicrobianos. De aumentar la incidencia de esta resistencia, adquiriría más importancia la vacuna contra neumococo y podrían ampliarse sus indicaciones (5). La vacuna se recomienda para los enfermos crónicos renales, pero la posibilidad de efectos adversos en las nefrosis es motivo de cautela por parte de algunos nefrólogos.

La vacuna en los niños menores de dos años hasta ahora no se ha encontrado que les produzca efectos peligrosos. No se recomienda en éstos por la insuficiente inmunidad que les ofrece. Se les puede administrar si hay una indicación importante, pero debe repetirse después de los dos años de edad.

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En los niños con esplenectomía la vacuna confiere protección contra muchas de las infecciones por neumococos pero dicha protección puede ser incompleta (6, 7). Por otra parte, se ha encontrado que la vacuna puede causar alguna inmunidad contra estreptococos del grupo B y gonococos (8).

El uso de la vacuna en la prevención de la otitis media depende de la severidad del problema y debe hacerse reconociendo que hay otros importantes agentes etiológicos de la otitis como el H influenzae (9). La vacuna protege contra los tipos 9, 14, 19 y 23 que son causas importantes de la otitis media en los niños. Se ha estimado que el 20 por ciento de los niños norteamericanos sufre de no menos de un ataque de otitis media por neumococos durante los primeros dos años de edad y que el 10 por ciento de los casos de otitis media aguda en niños es causado por neumococos.

### Conclusiones

La experiencia con la vacuna de neumococos en los niños es menor que en los adultos y hasta tanto se haya vacunado un número mayor de niños no es recomendable emplearla en la población pediátrica rutinariamente. Pero la vacuna no se está empleando en muchas de las personas de todas las edades que se pueden beneficiar de la misma y para las cuales está indicada. Esta situación se ha estudiado especulándose que obedece en gran parte a

apatía, temor o ignorancia tanto por parte del público como de la profesión médica (10). La vacuna está indicada en todo niño mayor de dos años de edad con enfermedad o defecto crónico que lo haga más susceptible a las infecciones por neumococos.

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### SCIATIC NERVE COMPRESSION WITH ANTICOAGULATION THERAPY

*Howard W. Wallach, MD, Mark E. Oreni, MA, Baptist Hospital of Miami and Department of Hematology & Oncology of the University of Miami. Arch of Neurol: 36: 448, 1979.*

Reporte de un caso de un paciente masculino de 62 años que padecía de esclerosis múltiple desde 1948 y páresis de la pierna izquierda por largo tiempo. Fue admitido al hospital debido a una flebitis femoral once días después de una resección transuretral para un carcinoma de la próstata y cinco días después de una orquiectomía bilateral. Terapia con anticoagulantes como la heparina y warfarina sódica resolvieron el problema de la flebitis en siete días. Para el día número 10 el paciente empezó a quejarse de un dolor en la cadera izquierda con radiación hacia la parte posterior del muslo. Envolvimiento metastásico fue descartado con gammagrafía de hueso. Para el día número 12 apareció una taquicardia de 100/min. El paciente se mantenía en la posición de cúbito lateral derecha debido al dolor que experimentaba en la nalga izquierda al asumir posición supina. Había algo de edema sobre el trocánter mayor, pero las áreas glúteas estaban simétricas. No se encontraron equimosis. Había dolor en el cuadrante inferior izquierdo y la región inguinal izquierda. Exquisito dolor se notaba a lo largo del nervio ciático izquierdo hasta la mitad del muslo. Los cambios neurológicos previos en la extremidad izquierda permanecieron iguales, sin cambio alguno. Las pruebas de coagulación estaban dentro de límites terapéuticos. El hematocrito bajó de 42 por ciento en la admisión a 34 por ciento para el día número 10.

Hematoma retroperitoneal con plexopatía lumbar se sospechó. Un IVP no demostró desviaciones de los ureteres o vejiga urinaria. CT Scan del espacio retroperitoneal y pelvis no demostró una masa en el

abdomen pero sí reveló una masa en los músculos glúteos izquierdos. El paciente se trató con sulfato de protamina y Vitamina K y su hematocrito se estabilizó en 28 por ciento. Los valores de las pruebas de coagulación regresaron a límites normales.

La hemorragia retroperitoneal es una complicación de la terapia con anticoagulantes y puede ocurrir aun cuando las pruebas de coagulación se encuentren dentro de límites terapéuticos. La compresión del plexo lumbar, en especial del nervio femoral, es una consecuencia de un hematoma en el psoas o el músculo ilíaco, o ambos. Usualmente aparece primero un dolor lumbar, abdominal o inguinal, seguido de signos más específicos de compresión nerviosa que incluyen dolor que radía al muslo, reflejos ausentes, debilidad y pérdida de sensaciones.

Grandes cantidades de sangre se pueden perder en el espacio retroperitoneal causando hipovolemia y shock. Como demuestra este caso, la pérdida de sangre también puede ocurrir entre los músculos glúteos y ser significativa.

Todo paciente que llegue con dolor en la cadera, muslo, o un hematocrito bajo y recibiendo terapia con anticoagulantes nos debe hacer pensar en la posibilidad de sangrado retroperitoneal en nalgas o muslo.

*(Sometido por Tomás Poventud, MD)*

### A PSYCHIATRIC STUDY OF PATIENTS WITH PERSISTENT LOW BACK PAIN

*G. G. Lloyd, S. N. Wolkind, R. Greenwood, and D. H. Harris: Rheumatology and Rehabilitation, 1979: 18, 30-34.*

La asociación del dolor a desórdenes psiquiátricos se reconoce frecuentemente en observaciones clínicas.



Este puede ser una manifestación de desorden de tipo síquico o en ocasiones ser el precipitante de las manifestaciones de desorden mental. Desde hace tiempo se han considerado factores psicológicos como posible etiología de dolor bajo de espalda y se han hecho estudios para probar esta teoría. El estudio actual se estableció para estimar la prevalencia de desorden psiquiátrico y tratar de predecir los que serían persistentes en sus quejas de dolor.

Se estudiaron pacientes con dolor de espalda, algunos con irradiación a una o ambas piernas, pero que no tuvieran factores de tipo orgánico del tipo de espondilitis anquilosante, neoplasias o trauma a columna vertebral.

Los pacientes fueron examinados de modo convencional y llevaron el "Middlesex Hospital Questionnaire" que se esperaba diera luz sobre posibles problemas mentales. Fueron manejados siguiendo criterios reumatológicos y evaluados, a la vez, por un psiquiatra quien no era enterado de los hallazgos ni el tratamiento de lo somático.

Entraron en el estudio 188 pacientes, de los cuales fueron seleccionados 31 como "persistentes" (su sintomatología no mejoró en 90 días). De éstos, 23 aceptaron ser estudiados y de entre ellos se encontró 8 con desorden de tipo depresivo, con problemas sociales y económicos clásicamente asociados a este diagnóstico. Hubo otros en los que hubo dudas sobre el diagnóstico, el cual no se determinó con certeza por la naturaleza del estudio.

La determinación psicológica de los pacientes no pudo predecir cuáles pacientes con dolor de espalda serían "persistentes". Sin embargo, se puede inferir del estudio que en muchos casos hay una asociación real de problemas de tipo psicológico con problemas persistentes de dolor bajo de espalda. No se puede hacer un cálculo exacto, pero los autores llaman la atención sobre el hecho de que entre los pacientes con dolor de espalda se pueden identificar sujetos que recibirían un máximo de beneficio con tratamiento psiquiátrico.

*(Sometido por Frank W. López, MD)*

## ARTHROGRAPHY — ASSISTED INTRAARTICULAR INJECTION OF STEROIDS IN TREATMENT OF ADHESIVE CAPSULITIS

*Joseph J. Weiss, MD, Y. Ming Ting, MD - Vol 59: 285-287, June, 1978 - Arch. Phys. Med. Rehabil.*

Una vez se haga la artrografía del hombro para establecer el diagnóstico de capsulitis adhesiva, se procede a inyectar esteroides a través de la aguja in situ del artrograma. Subsiguientes inyecciones intraarticulares de esteroides, si fueran necesarias, se dieron en la clínica externa utilizando el mismo sitio establecido cuando se hizo la artrografía. De 18 pacientes tratados de esta forma, 16 recobraron la función suficiente para poder volver al trabajo usual y sus actividades del diario vivir. En 11 pacientes, la mejoría estuvo asociada con un movimiento indoloro completo del hombro, en vez de un retorno del movimiento glenohumeral. Esta terapia aparenta ser preferida a otras formas de inyección intraarticular, y es una alternativa a la cirugía cuando la terapia física ha fallado.

*(Sometido por Rafael Seín, MD)*

## CRITERIA FOR DIAGNOSIS OF GUILLAIN-BARRE SYNDROME

*A. K. Asbury, G. W. Arnason, H. R. Karp. - Ann. Neurol 3: 565-566, 1978.*

Criterios para el diagnóstico del síndrome de Guillain-Barré han sido establecidos internacionalmente. Estos criterios ayudan al neurólogo y a los no neurólogos a reconocer el síndrome. El siguiente es un resumen de los criterios elaborados por los "Annals" de Neurología.

Es frecuente que a este síndrome le precedan situaciones como una infección viral, inoculación previa o cirugía; pero no es diagnóstico.

Se requieren para el diagnóstico:

I Debilidad motora progresiva de más de

una extremidad.

II Arreflexia - pérdida de reflejos tendinosos.

III Criterios que fuertemente sugieren el síndrome:

A. Clínicamente:

1. Debilidad motora progresiva con suspensión de esta progresión en cuatro semanas.
2. Simetría relativa.
3. Síntomas sensoriales leves.
4. Envolvimiento de pares craneales, especialmente el facial.
5. Recuperación generalmente a las dos o cuatro semanas, que siguen a la suspensión de debilidad motora progresiva.
6. Signos de disfunción autonómica.

B. Estudio del líquido cefalorraquídeo:

1. Proteínas elevadas en el líquido cefalorraquídeo después de la primera semana.
2. Menos de 10 leucocitos mononucleares por mm<sup>3</sup>.

C. Electrodiagnóstico:

1. El 80 por ciento tendrá velocidad de conducción nerviosa lenta.
2. No se afectan todos los nervios
3. La latencia distal de los nervios se afecta más que la proximal y se aumenta.
4. Estudios de conducción no se hacen anormales hasta varias semanas después de la enfermedad.

(Sometido por Alfredo Vélez Ponce, MD)

## SIGNIFICANCE OF CHRONIC BIFASCICULAR BLOCK WITHOUT APPARENT ORGANIC HEART DISEASE

*Dhingra R. C., Wyndham, C., Bauvernfeind, R., Denes P., et al: Circulation 60: 33, 1979.*

En este estudio prospectivo se siguen 452 pacientes con bloqueo bifascicular un promedio de 3.3 años. Ochenta y seis (19 por ciento) de estos pacientes no tienen evidencia clínica de otra enfermedad orgánica de corazón y se denominaron enfermedad de conducción primaria (ECP). El resto tenía evidencia de enfermedad orgánica del corazón (EOC). Los pacientes con ECP tenían menor incidencia de angina, disnea, fallo congestivo, cardiomegalia, y prematuros ventriculares como parte del diseño del estudio. Al comparar ambos grupos los pacientes con ECP tenían intervalos AH y HV menos prolongado que los pacientes con EOC. Al seguimiento, la incidencia de muerte súbita, muerte cardiovascular y bloqueo atrioventricular espontáneo fue más baja en los pacientes con ECP. Los pacientes con ECP tienen menos anomalías electrofisiológicas, bloqueo atrioventricular espontáneo, muerte súbita y muerte cardiovascular que los pacientes con EOC que tienen enfermedad bifascicular similar.

(Sometido por G. Cintrón, MD, VAH)

## "TENNIS ELBOW", EVALUACION, TRATAMIENTO Y PREVENCIÓN

*La Freniere, J. G.: Physical Therapy, 59:6 - 742-746, June, 1979.*

Aunque el "tennis elbow" puede ser ocasionado por otras actividades que envuelven contracciones violentas de los extensores de la muñeca combinado con movimientos de supinación, tales como un saludo vigoroso de la mano, el apretar un tornillo, el usar una llave inglesa, y otros movimientos similares, este artí-

culo concentra fundamentalmente en lesiones del codo producidas en el jugador de tenis. Con el interés que permea al individuo de nuestra sociedad hoy día de encontrarse capacitado físicamente y de utilizar el tiempo libre en la recreación, es de esperar que el médico y su terapeuta estén capacitados para rehabilitar al paciente en los niveles que él necesita para participar en varias y diversas actividades extracurriculares.

Este artículo asistirá al médico y a su terapeuta físico en solucionar y aplicar un tratamiento propio a este desorden comunmente llamado "tennis elbow". En él la información (1) ofrece directrices para determinar la causa del dolor; (2) asiste en escoger un plan de tratamiento diferencial; (3) delinea un completo, efectivo y detallado programa de rehabilitación e (4) incluye un programa preventivo e informativo para el médico, el terapeuta y su paciente.

(Sometido por Rafael Alvarez, MD)

## FRACTURES IN PATIENTS WITH MYOPATHY

Hirota, H., Doko, S., Fukunaga, H., Yamamoto, I., Morita, R., Torizuka, K., Yoshioka, C.: *Arch Phys Med Rehabil* 60: 178-182, 1979

Durante un período de 4 años, se encontraron 15 fracturas en 10 pacientes con miopatías entre un total de 48 pacientes hospitalizados con miopatías. Los sitios predominantes de fracturas fueron el fémur (interecondilar) y el húmero (sub-capital). Determinando el volumen total de potasio en el organismo, el contenido mineral óseo, calcio sérico, fósforo inorgánico, 25-OH vitamina D<sub>3</sub>, hormona paratiroidea y la calcitonina se concluyó que la tendencia a ocurrir fracturas en los pacientes miopáticos es producida por atrofia ósea, debido a falta de tensión muscular, lo cual se relaciona a una disminución del volumen muscular.

(Sometido por Jesús A. Maldonado, MD)

## PRONOSTICO DEL RECIEN NACIDO CON TRANSPOSICION DE LOS GRANDES VASOS

Gutgesell, H. P., Garson, A., McNamara, D. G.: *Am. J. of Cardiol* 44: 96, julio 1979

Se analiza la data de 112 neonatos consecutivos con transposición de los grandes vasos (TGV). El manejo fue uniforme: cateterismo cardíaco con septotomía de balón en el período neonatal, cirugía paliativa en el primer año en los casos necesarios y luego reparación quirúrgica utilizando el procedimiento de Mustard.

La mortalidad en el período neonatal fue de 8 por ciento. Entre este período y la operación de Mustard a 28 de ellos (38 por ciento) fue necesario someterlos a cirugía paliativa y 10 (14 por ciento) murieron o tuvieron complicaciones médicas graves. La mortalidad en el momento del procedimiento de Mustard fue de 14 por ciento (10 de 71). Cuando este procedimiento se lleva a cabo en los primeros 3 meses de vida el riesgo es mayor al igual que la incidencia de complicaciones.

Las secuelas y residuos hemodinámicos y electrofisiológicos en el período postoperatorio tardío es de 20-30 por ciento con mortalidad de 8 por ciento.

La data indica que 50 por ciento de los neonatos con TGV sobreviven 5 años con una función excelente y un 15-20 por ciento sobreviven con impedimentos médicos.

(Sometido por Rafael Villavicencio, MD)

## CLINICAL INDICATORS OF LEFT MAIN CORONARY ARTERY DISEASE IN UNSTABLE ANGINA

Plotnick GD, Greene HL, Carliner NH et al — *Annals of Internal Medicine* 91: 149, 1979.

## NON INVASIVE IDENTIFICATION OF LEFT MAIN AND THREE VESSEL CORONARY



**ARTERY DISEASE BY MYOCARDIAL STRESS PERFUSION SCINTIGRAPHY AND TREADMILL EXERCISE ELECTROCARDIOGRAPHY**

*Dash H, Massie BM, Botvinick EH, et al — Circulation 60: 276, 1979.*

En lo único que han estado de acuerdo *todos* los estudios comparando supervivencia médica vs cirugía en enfermedad coronaria es que los pacientes con enfermedad del tronco mayor de la coronaria izquierda tienen mejor supervivencia en tratamiento por cirugía. El primero de estos artículos indica que en pacientes con el cuadro clínico de angina inestable los únicos variables clínicos que apuntan a enfermedad del tronco mayor son: angina progresiva asociada con cambios transitorios de depresión del segmento ST en las derivaciones anteriores e inferiores simultáneas o calcificación del tronco mayor en fluoroscopia. Aun estos factores tienen poca sensibilidad y valor predictivo. El segundo estudio trata de correlacionar electrocardiografía y scintigrafía al ejercicio con enfermedad del tronco mayor. Cuando ambas técnicas se usan en conjunto, una prueba altamente positiva (EKG con  $> 2\text{mm}$  ST deprimido antes del 3er estadio de ejercicio o scintigrama al ejercicio con defectos de perfusión en el septo interventricular y pared anterior y postero-lateral) identificó solo el 60 por ciento de los pacientes con enfermedad del tronco mayor izquierdo aunque la especificidad fue 90 por ciento. Hoy en día no hay pruebas no-invasivas confiables para detección certera de enfermedad del tronco mayor. Los factores clínicos y las pruebas mencionadas

pueden servir de guía pero no eliminan ni suplantán arteriografía coronaria en el caso que se sospecha enfermedad del tronco mayor.

*(Sometido por Guillermo Cintrón, MD)*

**CORRELATION OF THE CAT-SCAN AND VISUAL DEFECTS IN VASCULAR LESIONS OF THE POSTERIOR VISUAL TRACTS**

*McAulay, D. L., Russell, W. R.: Journal of Neurol. Neuros. and Psych. 42 - 4: 298-311, 1979.*

Treinta y nueve pacientes con diversos tipos de hemianopsias homónimas aisladas como resultado de lesiones isquémicas en la parte posterior del hemisferio cerebral fueron examinados por tomografía computarizada. La mayor parte tenían lesiones de baja intensidad localizadas en la distribución de la arteria cerebral posterior. La localización de estas lesiones se correlacionó con los defectos en los campos visuales. Las lesiones que daban lugar a defectos de cuadrantes eran más pequeñas que las que causaban hemianopsias. Los defectos de cuadrante inferior ocurrían en la parte superior y vice-versa. El hecho de que no se envolviera la mácula fue asociado con la supervivencia del polo occipital en algunos casos. Los casos bilaterales tenían una prevalencia más alta de defectos asociados.

*(Sometido por Jesús A. Maldonado, MD)*

### THIRD PEDIATRIC NEPHROLOGY SYMPOSIUM

Will be sponsored by Georgetown University and the San Juan City Hospital, at the Caribe Hilton Hotel, San Juan, Puerto Rico, December 4-8, 1979.

Topics include: Fluid and Electrolytes, Nephrological Emergencies, Recent Advances, Pediatric Urology, Hypertension. Speakers are internationally known in the field of Nephrology. Accreditation in Category I for the Physician's Recognition Award has been applied for. Tuition: \$160 for physicians in practice; \$75 physicians in training with letter from chief of service.

For information write: José F. Pascual, MD, P. O. Box 3342, Old San Juan, Puerto Rico 00904.

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**CONSENSUS DEVELOPMENT CONFERENCE ON "THE USE OF MICROPROCESSOR-BASED 'INTELLIGENT' MACHINES IN PATIENT CARE"** - Sponsored by National Institutes of Health, Division of Research Services.

**To Discuss:**

Recent advances in the use of "intelligent" machines in patient care.

The prospects for future developments in the area.

Related social, legal, and ethical issues.

When: October 17-19, 1979

Where: Sheraton Silver Spring Motor Hotel, 8727 Colesville Road, Silver Spring, Maryland 20910

Preliminary approval for 5 hours of AMA Category I Credit.

For additional information contact: Henry S. Eden, MD, Assistant to the Chief, Biomedical Engineering and Instrumentation Branch, DRS, Building 13, Room 3W 13, National Institutes of Health, Bethesda, Maryland, 20205 (301) 496-5771.

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### CLINICAL CYTOPATHOLOGY FOR PATHOLOGISTS - POSTGRADUATE COURSE

The Twenty-first Postgraduate Institute for Pathologists in Clinical Cytopathology is to be given at The Johns Hopkins University School of Medicine and The Johns Hopkins Hospital, Baltimore, Maryland, April 14-25, 1980. The full two week program is designed for Pathologists who are Certified (or qualified), by the American Board of Pathology (PA), or their international equivalents.

It will provide an intensive refresher in all aspects of the field of Clinical Cytopathology, with time devoted to newer techniques, special problems, and recent applications. Topics will be covered in lectures, explored in small informal conferences, and discussed

over the microscope with the Faculty. Self-instructional material will be available to augment at individual pace. A loan set of slides with text will be sent to each participant for home-study during March and April before the Institute. Credit hours 120 in AMA Category I.

Application is to be made before March 7, 1980. For details, write: John K. Frost, MD, 610 Pathology Building, The Johns Hopkins Hospital, Baltimore, Maryland 21205, U. S. A.

The entire Course is given in English.

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#### AMERICAN COLLEGE OF CARDIOLOGY EXTRAMURAL PROGRAMS

1979

- |             |  |
|-------------|--|
| Sept. 10-13 | Electrocardiography: Core Curriculum and Self-Assessment, Indianapolis, Ind.             |
| Sept. 10-13 | Electrocardiography: Core Curriculum and Self-Assessment, San Francisco, Calif.          |
| Sept. 17-19 | Advanced Echocardiography, Indianapolis, Ind.  |
| Oct. 11-13  | New Concepts in Management of Congestive Heart Failure, Kiawah Island, Charleston, S. C. |
| Oct. 18-20  | Cardiology Update-1979, Monterey, Calif.   |

- |            |   |
|------------|---|
| Oct. 22-23 | Correlations in Ischemic Heart Disease, Chapel Hill, N. C.  |
| Oct. 25-27 | New Techniques and Concepts in Cardiology. Coronary Artery Disease: Rehabilitation, Surgery, Coronary Spasm, Balloon Dilatation; Valvular Heart Disease; Hypertrophic Cardiomyopathy, Washington, D. C. |
| Nov. 5-14  | Cardiology for the Consultant: A Clinician's Retreat, Rancho Santa Fe, Calif.   |
| Dec. 2-5   | Coronary, Valvular, Hypertensive and Myocardial Heart Diseases: The Multidisciplinary Approach, Williamsburg, Va.   |
| Dec. 7-9   | Advances in Heart Disease 1980-12th Annual Seminar on Clinical Cardiology, San Francisco, Calif.  |
| Dec. 12-14 | Cross - Sectional Echocardiography vs. Cardiac Nuclear Imaging, Philadelphia, Pa.   |
| Dec. 14-16 | Clinical Decisions in Cardiovascular Disease: Diagnosis, Prevention and Therapy, New York, N. Y.  |

Send application for enrollment to:

Registration Secretary  
Extramural Programs Department  
American College of Cardiology  
9111 Old Georgetown Road  
Bethesda, Md., 20014





A reminder

# ZYLOPRIM<sup>®</sup> (allopurinol)

100 and 300 mg scored Tablets

- inhibits uric acid formation
- helps prevent urate crystal depositions in synovia
- reduces risk of uric acid lithiasis

**INDICATIONS AND USE:** This is not an innocuous drug and strict attention should be given to the indications for its use. Pending further investigation, its use in other hyperuricemic states is not indicated at this time.

Zyloprim<sup>®</sup> (allopurinol) is intended for:

1. treatment of gout, either primary, or secondary to the hyperuricemia associated with blood dyscrasias and their therapy;
2. treatment of primary or secondary uric acid nephropathy, with or without accompanying symptoms of gout;
3. treatment of patients with recurrent uric acid stone formation;
4. prophylactic treatment to prevent tissue urate deposition, renal calculi, or uric acid nephropathy in patients with leukemias, lymphomas and malignancies who are receiving cancer chemotherapy with its resultant elevating effect on serum uric acid levels.

**CONTRAINDICATIONS:** Use in children with the exception of those with hyperuricemia secondary to malignancy. The drug should not be employed in nursing mothers.

**Patients who have developed a severe reaction to Zyloprim should not be restarted on the drug.**

**WARNINGS:** ZYLOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR ANY SIGN OF ADVERSE REACTION. In some instances a skin rash may be followed by more severe hypersensitivity reactions such as exfoliative, urticarial and purpuric lesions as well as Stevens-Johnson syndrome (erythema multiforme) and very rarely a generalized vasculitis which may lead to irreversible hepatotoxicity and death.

A few cases of reversible clinical hepatotoxicity have been noted and in some patients asymptomatic rises in serum alkaline phosphatase or serum transaminase have been observed. Accordingly, periodic liver function tests should be performed during the early stages of therapy, particularly in patients with pre-existing liver disease. Patients should be alerted to the need for due precautions when engaging in activities where alertness is mandatory.

Nevertheless, iron salts should not be given simultaneously with Zyloprim. This drug should not be administered to immediate relatives of patients with idiopathic hemochromatosis.

**In patients receiving Purlinethol<sup>®</sup> (mercaptopurine) or Imuran<sup>®</sup> (azathioprine), the concomitant administration of 300-600 mg of Zyloprim per day will require a reduction in dose to approximately one-third to one-fourth of the usual dose of mercaptopurine or azathioprine. Subsequent adjustment of doses of Purlinethol or Imuran should be made on the basis of therapeutic response and any toxic effects.**

**Usage in Pregnancy and Women of Childbearing Age.** Zyloprim<sup>®</sup> (allopurinol) should be used in pregnant women or women of childbearing age only if the potential benefits to the patient are weighed against the possible risk to the fetus.

**PRECAUTIONS:** Some investigators have reported an increase in acute attacks of gout during the early stages of allopurinol administration, even when normal or sub-normal serum uric acid levels have been attained.

It has been reported that allopurinol prolongs the half-life of the anticoagulant, dicumarol. This interaction should be kept in mind when allopurinol is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.

A fluid intake sufficient to yield a daily urinary output of at least 2 liters and the maintenance of a neutral or, preferably, slightly alkaline urine are desirable to (1) avoid the theoretic possibility of formation of xanthine calculi under the influence of Zyloprim therapy and (2) help prevent renal precipitation of urates in patients receiving concomitant uricosuric agents.

Patients with impaired renal function require less drug and should be carefully observed during the early stages of Zyloprim administration and the drug withdrawn if increased abnormalities in renal function appear.

In patients with severely impaired renal function, or decreased urate clearance, the half-life of oxipurinol in the plasma is greatly prolonged. Therefore, a dose of 100 mg per day or 300 mg twice a week, or perhaps less, may be sufficient to maintain adequate xanthine oxidase inhibition to reduce serum urate levels. Such patients should be treated with the lowest effective dose, in order to minimize side effects.

Mild reticulocytosis has appeared in some patients.

As with all new agents, periodic determination of liver and kidney function and complete blood counts should be performed especially during the first few months of therapy.

## ADVERSE REACTIONS:

**Dermatologic:** Because in some instances skin rash has been followed by severe hypersensitivity reactions, it is recommended that therapy be discontinued at the first sign of rash or other adverse reaction (see WARNINGS). Skin rash, usually maculopapular, is the adverse reaction most commonly reported.

Exfoliative, urticarial and purpuric lesions, Stevens-Johnson syndrome (erythema multiforme) and toxic epidermal necrolysis have also been reported.

A few cases of alopecia with and without accompanying dermatitis have been reported.

In some patients with a rash, restarting Zyloprim (allopurinol) therapy at lower doses has been accomplished without untoward incident.

**Gastrointestinal:** Nausea, vomiting, diarrhea, and intermittent abdominal pain have been reported.

**Vascular:** There have been rare instances of a generalized hypersensitivity vasculitis or necrotizing angitis which have led to irreversible hepatotoxicity and death.

**Hematopoietic:** Agranulocytosis, anemia, aplastic anemia, bone marrow depression, leukopenia, pancytopenia and thrombocytopenia have been reported in patients, most of whom received concomitant drugs with potential for causing these reactions. Zyloprim<sup>®</sup> (allopurinol) has been neither implicated nor excluded as a cause of these reactions.

**Neurologic:** There have been a few reports of peripheral neuritis occurring while patients were taking Zyloprim. Drowsiness has also been reported in a few patients.

**Ophthalmic:** There have been a few reports of cataracts found in patients receiving Zyloprim. It is not known if the cataracts predated the Zyloprim therapy. "Toxic" cataracts were reported in one patient who also received an anti-inflammatory agent; again, the time of onset is unknown. In a group of patients followed by Gutman and Yü for up to five years on Zyloprim therapy, no evidence of ophthalmologic effect attributable to Zyloprim was reported.

**Drug Idiosyncrasy:** Symptoms suggestive of drug idiosyncrasy have been reported in a few patients. This was characterized by fever, chills, leukopenia or leukocytosis, eosinophilia, arthralgias, skin rash, pruritus, nausea and vomiting.

**OVERDOSAGE:** Massive overdosing, or acute poisoning, by Zyloprim has not been reported.

**HOW SUPPLIED:** 100 mg (white) scored tablets, bottles of 100 and 1000; 300 mg (peach) scored tablets, bottles of 30, 100 and 500. Unit dose packs for each strength also available.

Complete information available from your local B. W. Co. Representative or from Professional Services Department PML.

U.S. Patent No. 3,624,205 (Use Patent)



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Research Triangle Park  
North Carolina 27709

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Tagamet

THE UPJOHN COMPANY

Motrin

**Tenuate®**  
(diethylpropion hydrochloride NF)

**Tenuate Dospan®**  
(diethylpropion hydrochloride NF) controlled-release

### AVAILABLE ONLY ON PRESCRIPTION

#### Brief Summary

**INDICATION:** Tenuate and Tenuate Ospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence:* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSAGE AND ADMINISTRATION:** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Ospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSAGE:** Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phenolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.  
Cayey, Puerto Rico 00633

Direct Medical Inquiries to:

MERRELL-NATIONAL LABORATORIES  
Division of Richardson-Merrell Inc.  
Cincinnati, Ohio 45215, U.S.A.

Licensor of Merrell®

**References:** 1. Citations available on request—Medical Research Department, MERRELL RESEARCH CENTER, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga, M.T., O'illon, R.H., and Leyland, H.M.: A Comprehensive Review of Diethylpropion Hydrochloride. International Symposium on Central Mechanisms of Anorectic Drugs, Florence, Italy, Jan. 20-21, 1977.

**Merrell**



**Overweight may not always be simple...  
complications can develop.\***

**Complicated or not...**

# **Tenuate<sup>®</sup> Dospan<sup>®</sup> <sup>IV</sup>** **(diethylpropion hydrochloride NF)** **75 mg. controlled-release tablets**

## **A useful short-term adjunct in an indicated weight loss program.**

Overweight patients in certain diagnostic categories often require strict appetite control and a successful program of weight reduction may tend to diminish the incidence or severity of the complications in some patients. Diethylpropion hydrochloride has been reported useful in such patients and while it is not suggested that Tenuate itself in any way reduces the complications of overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. **Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.**

## **In uncomplicated overweight.**

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

## **Clinical effectiveness.**

The anorectic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.<sup>1</sup> And the unique chemistry of Tenuate provides "...anorectic potency with minimal overt central nervous system or cardiovascular stimulation."<sup>2</sup> Compared with the amphetamines, diethylpropion has minimal potential for abuse.

**Tenuate—it makes sense.  
And it's responsible medicine.**

\*Studies have shown that obesity is associated with an increased incidence of hypertension, symptomatic heart disease, adult-onset diabetes, and other diseases.

# **Merrell**



For prescribing information see opposite page



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600 mg tablets  
**Motrin**<sup>®</sup>  
ibuprofen, Upjohn

More convenient for  
some of your patients.

Now there are three  
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600 mg, 400 mg, and 300 mg



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J-6999-4

April 1



# Tagamet®

brand of

## cimetidine

### How Supplied:

Pale green 300 mg. tablets  
in bottles of 100 and Single Unit Packages of 100  
(intended for institutional use only).

Injection, 300 mg./2 ml.,  
in single-dose vials  
and in 8 ml. multiple-dose vials,  
both in packages of 10.

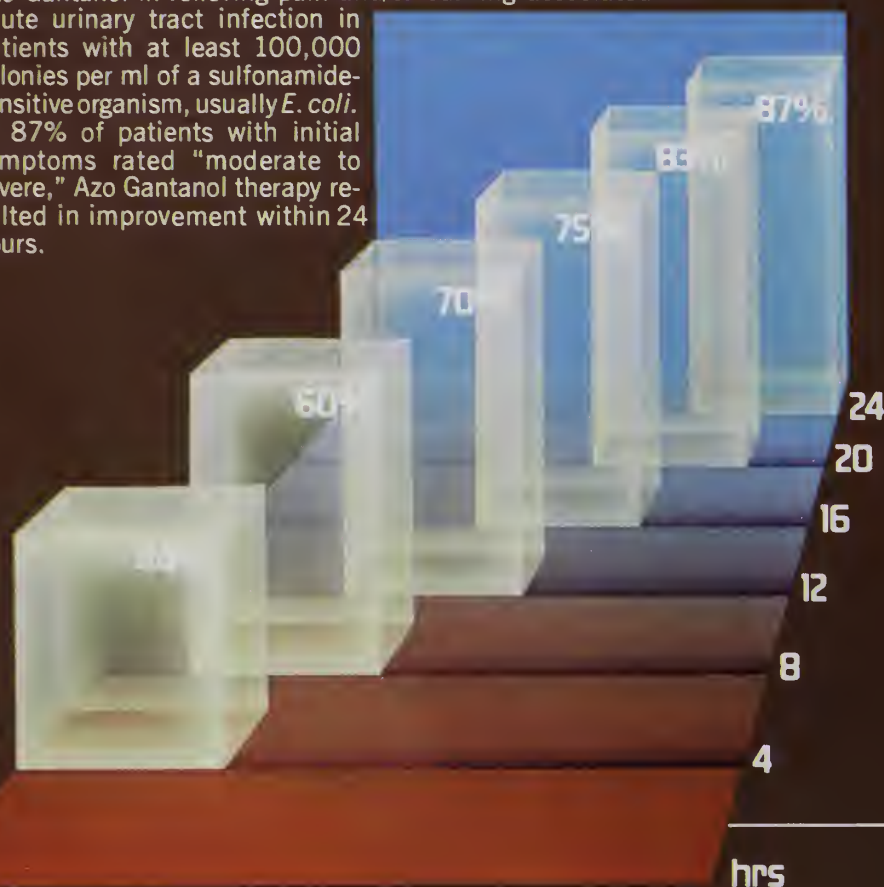
**SK&F LAB CO.**  
a SmithKline company



## Important data on the pain of acute cystitis:

# In 87% of patients studied (303 of 349), Azo Gantanol® reduced pain and/or burning within 24 hours\*

A controlled, multicenter study assessed the efficacy of Azo Gantanol in relieving pain and/or burning associated with acute urinary tract infection in patients with at least 100,000 colonies per ml of a sulfonamide-sensitive organism, usually *E. coli*. In 87% of patients with initial symptoms rated "moderate to severe," Azo Gantanol therapy resulted in improvement within 24 hours.



Before prescribing, please consult complete product information, a summary of which follows: Indications: In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. Note: Fully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; aminobenzoic acid to follow-up culture media. Increasing frequency of resistant organisms limit the usefulness of antibacterials including sulfonamides. Measure sulfonamide blood levels: variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G disturbances.

**Warnings:** Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** Blood dyscrasias (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); allergic reactions (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I.* reactions (nausea, emesis, abdominal pain, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS* reactions (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *Miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

**Dosage:** Azo Gantanol is intended for the acute painful phase of urinary tract infections. Usual adult dosage: 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

**NOTE:** Patients should be told that the orange dye (phenazopyridine HCl) will color the urine.

**Supplied:** Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

**ROCHE** Roche Laboratories  
Division of Hoffmann-La Roche  
Nutley, New Jersey 07110

Fast pain relief plus effective antibacterial action

# Azo Gantanol®

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

for  
the pain

for  
the pathogens



## N O T I C I A S

### *NEWS FROM MEDIC ALERT FOUNDATION INTERNATIONAL*

#### *Intraocular Lens Implant Patients Need Medic Alert Protection*

With the new method of treating cataracts with intraocular lens implant, a warning for those who do have implants has been issued by Warren F. Smith, MD, ophthalmologist and Assistant Professor, Rush Medical School. Dr. Smith warns patients that have intraocular implants that indirect dilation of the pupils may be harmful. The implants may dislodge (dislocate) and vision will be altered.

He further goes on to state that approximately 250,000 intraocular lenses have been inserted to date. It is anticipated that there will soon be about 100,000 implanted each year for several years to come. He advised Medic Alert membership for all persons who have had intraocular implants. The bracelet should state "Intraocular Lens Implant" and the patients record should give date of implant and the type of manufacturer if known.

The general medical and surgical physician, particularly anesthesiologists and the neurological specialists, should be knowledgeable regarding the possible added problems in those patients wearing Medic Alert devices with this warning.

Medic Alert Foundation International is a non-profit, charitable and tax-exempt organization that provides a unique system of medical identification. Its purpose is to provide fast, accurate information to assist in the diagnosing and treating of individuals with hidden medical problems in emergency medical situations.

Serious allergies, diabetes, and epilepsy are a few

of the many diseases or conditions why people become members of Medic Alert. When a member cannot communicate his or her problem in an emergency because of unconsciousness, or any other reason, the Medic Alert emblem speaks for that person. It helps to prevent tragic or even fatal mistakes that can be made in emergency treatment if the patient has a hidden medical problem. It is equally valuable in assisting emergency personnel to deliver effective medical treatment.

For more information, write Medic Alert, P. O. Box 1009, Turlock, California 95380.

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#### *AMA NEWS:*

#### *BASKETBALL'S DUNKERS SUFFER HAND INJURIES*

CHICAGO — The young giants of the basketball court often run roughshod over smaller opponents, but the super tall boys have a unique accident hazard—the Dunk Laceration.

The Dunk Laceration means cuts on the hands encountered in "dunking" the basketball into the rim of the hoop. The rough edges of the loop cause the damage. The injury is unique among players who are tall enough and agile enough to leap up and push the ball down into the basket, rather than toss it from below as the smaller players must do.

Arthur R. Kirk, MD, of Portsmouth, VA., reports in the Aug. 3 Journal of the American Medical Associa-

tion on two young men injured during a basketball tournament. One had a deep cut requiring sutures on the side of the hand, and the other had a similar laceration.

The baskets were taken down and examined. The flange back of the rim caused the cuts. The underside had a sharp edge. Other jagged spots were found on the rim.

Says Dr. Kirk:

"In the interest of good sports medicine, all high school and college coaches, athletic directors, and attending physicians should check these basketball goals to prevent further injuries to players."

"All workers known to have been exposed to asbestos in the past, whether in shipyards, insulation work, factories, construction trades, brake repair, maintenance work, or otherwise, should be advised never to smoke, or, if they are smoking, to stop as soon as possible," they declare.

It had been known for ten years that some cancer deaths associated with prior asbestos exposure might be related to more than asbestos alone, the editorial points out. Drs. Selikoff and Hammond followed up 12,051 asbestos workers for ten years to determine the new statistics published in the editorial.

#### ASBESTOS PLUS CIGARETTES BOOSTS RATE OF LUNG CANCER

CHICAGO — Exposure to asbestos increases the risk of lung disease somewhat, but it is the combination of smoking and asbestos that causes most of the problem, says an editorial in the Aug. 3 Journal of the American Medical Association.

Irving J. Selikoff, MD, Mount Sinai School of Medicine of the City University of New York, and E. Cuyler Hammond, ScD, of the American Cancer Society, declare:

Death rates for lung cancer per 100,000 man-years, standardized for age, are as follows: 11.3 for men who neither worked with asbestos nor smoked cigarettes, 58.4 for men who worked with asbestos but did not smoke; 122.6 for cigarette smokers who had not worked with asbestos, and 601.6 for "those unfortunate enough to have both exposures — cigarettes and asbestos".

Asbestos by itself increases the risk of lung cancer by four or five times, but as the base risk is low this does not mean many cases, Drs. Selikoff and Hammond point out. Smoking itself causes a major increase in lung cancer, and when that high risk is multiplied manyfold, an immense increase is found.

#### PILL BOTTLE SAFETY CAPS DEFY MANY ADULTS

CHICAGO — The dialogue on the problems of adults in trying to open the child-resistant safety caps on pill bottles continues in the July 27 Journal of the American Medical Association.

A California pharmacist writes that "pharmacists should offer their elderly patients the option of having a non-child-resistant container" because many elderly persons have difficulty in removing the safety caps.

Says Gail S. Geiger, Pharm. D., of Huntington Memorial Hospital, Pasadena:

"Elderly patients have related many instances to me describing their dilemma in trying to open their prescription containers and the variety of instruments they have used in the process: pliers, hammer, screwdriver, hand-operated can openers and feet. One patient claimed that stomping on his bottle worked to free its contents.

"Another patient stated that her 7-year-old granddaughter could open her bottle when she, herself, could not."

Elderly patients should be routinely screened by druggists to determine whether they can manage the child-resistant safety cap. If they have a problem, a simpler cap may be substituted, Dr. Geiger says.

In another communication, Matilda S. McIntire, MD, and Carol R. Angle, MD, of the American Asso-

ciation of Poison Control Centers, Omaha, also urge that health professionals caring for the elderly demonstrate the container's proper use, and test the patient's ability to open the cap.

The safety caps have brought a marked reduction in incidence of accidental poisoning of small children from pills and other medicines but the safety caps also have been such a problem to some adults that they give up and neglect taking their medications.

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#### *PIANO PLAYING IS NEW HEALTH HAZARD*

CHICAGO — In the late 1970s scientists and consumerists are finding that many things in the world around us are hazardous to our health. This week comes a new hazard — playing the piano.

An occupational hazard of professional pianists is Carpal Tunnel Syndrome, an ailment that brings sharp pain to the wrist and fingers, says a communication in the July 27 Journal of the American Medical Association.

Playing the piano through years of heavy practice brings repeated shock to the fingers and arms, Joe S. Rosen, MD, of Northridge Hospital Foundation, Northridge, Calif., points out. Nerves in the wrist and fingers are damaged, causing the Carpal Tunnel Syndrome.

Treatment involves splinting the fingers and wrist to put the joints at rest, and injection of steroids. If these measures fail, sometimes surgery is required.

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#### *WINDOWLESS ROOMS AFFECT EMOTIONAL HEALTH*

CHICAGO — Windowless rooms may definitely be hazardous to your emotional health, says an editorial in the July 27 Journal of the American Medical

Association.

The problem is not lack of ventilation or illumination — these are taken care of by air conditioning and artificial lighting — but the absence of an outlet for human visual curiosity, the editorial points out.

One study is cited in which researchers found postoperative delirium more than twice as common among patients in windowless rooms. Both patients and staff in intensive therapy units in another study showed evidences of stress caused by deprivation of visual stimuli from the outside world. One researcher recommends "that windowless rooms be condemned out of hand, be they in hospital, office or factory."

"Windows are more than panes and frames," says the editorial. "They are a break in the walls, which symbolize repression, an escape from the visual prisons of enclosed spaces. Poets linked them in metaphor with the soul and the eye. Physicians cannot ignore them."

The editorial is by Samuel Vaisrub, MD, a senior editor of the Journal.

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#### *SURGERY PATIENTS TRANSFUSED WITH THEIR OWN BLOOD*

CHICAGO — The safest and best blood for a transfusion is your own.

In some communities it is now possible for an individual preparing for an operation to go to the hospital several times in prior months to donate blood. The blood is kept in cold storage, and brought out ready to use if needed during or after the surgery.

In the June 22 Journal of the American Medical Association Arthur J. Silvergleid, MD, of the Blood Bank of San Bernardino & Riverside Counties, California, reports on 103 individuals who prepared for their operations by donating up to three pints of blood each in advance.

The operations were varied — spinal fusion, breast augmentation, mastectomy, hip replacement, knee replacement, hysterectomy and others.



For those who needed blood, their own fluid served in most instances. In a few cases of severe bleeding, additional blood from the bank was required to supplement the individual's own supply.

There were no transfusion reactions among the 103 individuals. An occasional reaction when someone else's blood is infused occurs. There also was no transfer of hepatitis, an ever present risk in blood transfusions.

This technique is unquestionably the safest blood transfusion method available, says Dr. Silvergleid.

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#### *NEW TREATMENT SUCCEEDS FOR WIDESPREAD VENEREAL DISEASE*

CHICAGO — A successful treatment for a heretofore resistant form of venereal disease that is widespread in this country is described in the June 29 Journal of the American Medical Association.

The disease — genital herpes simplex infection — accounts for some 13 percent of all venereal disease in the United States, says Herbert A. Blough, MD, of the University of Pennsylvania, Philadelphia.

The treatment is with 2-deoxy-D-glucose.

Thirty-six women with genital herpes infections were treated with 2-deoxy-D-glucose for a three-week period in a study conducted in Philadelphia. In those with a first infection, 95 per cent were successfully cured, with two recurrences after 24 months, Dr. Blough says. Among those with recurrent infections, 90 per cent had notable improvements. In the first infections, discomfort cleared within 12 to 72 hours of therapy, and 90 per cent of the patients were free of symptoms in our days, he says.

The substance acts to interfere with the multiplication of the herpes virus. It was first-used in research studies to treat virus infection in rabbits.

Genital herpes simplex infection is a serious medical problem because there has been no effective agent to combat the infection, and because the virus may spread to the fetus at the time of delivery. The

disease also is associated with cancer of the cervix.

It had been known for almost 20 years that 2-deoxy-D-glucose would block growth of viruses in the laboratory, but its use to treat human infection had not heretofore been explored, Dr. Blough says.

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#### *TICK-BORNE RELAPSING FEVER SPREADS OVER U. S.*

CHICAGO — An unusual tick-borne disease, relapsing fever, is now occurring in the western United States and recently a case was documented in the east, says a report in the June 29 Journal of the American Medical Association.

There are two forms of relapsing fever, louse-borne and tick-borne, says Michael D. Malison, MD, of Huntington Memorial Hospital, Pasadena, California.

The louse-borne variety is found in other parts of the world, but the only case reported in the United States was in a recent immigrant from Ethiopia, Dr. Malison says. Tick-borne relapsing fever is spread in the U. S. by ticks on small rodents — rats, mice, chipmunk and squirrels. The ticks themselves are of a variety that feeds on the blood of their host for five to 20 minutes, then drop off. Thus the infected individual does not find a tick and usually does not know he or she has been bitten.

Dr. Malison describes two cases in which women became ill after vacationing in resort cabins in California.

Diagnosis requires a blood test. Usually the fever is self-limiting, but recovery can be speeded by treatment. Prevention is aimed at controlling the rodents and the ticks. Fumigation of any rustic cabin periodically is recommended.

## MEDICINE

CHICAGO — The 21st American Medical Association Conference on the Medical Aspects of Sports will be held next Jan. 12 at San Antonio.

“Sports Medicine for the Primary

“Sports Medicine for the Primary Care Physician” will be the theme of the conference.

Sports medicine experts from across the nation will discuss such topics as women in sports, the physical exam for the young athlete, heart evaluation of the young athlete, elbow injuries in young ball players, knee injuries, back injuries, injuries to the hand, the role of radiology and nuclear medicine in evaluating athletic injuries, prevention of injuries and violence in sports.

Keynote luncheon speaker for the conference will be Kenneth H. Cooper, MD, executive director of the Aerobics Center, The Cooper Clinic, Dallas. Dr. Cooper is a national authority on exercise and physical conditioning.

Program participants will include Leatha Y. Hunter, MD, orthopedic surgeon, University of Mi-

chigan, Ann Arbor; Donald L. Cooper, MD, team physician, Oklahoma State University, Stillwater; William B. Strong, MD, pediatric cardiologist, Medical College of Georgia, Augusta; Kay E. Wilkins, MD, orthopedic surgeon, University of Texas Medical School, San Antonio.

Bernard R. Cahill, MD, orthopedic surgeon, Peoria, Ill.; Arvo Neidre, MD, orthopedist, University of Texas Medical School, San Antonio; Jerry D. Julian, MD, orthopedic surgeon for the athletic department of the University of Texas, Austin; Frank C. McCue, MD, orthopedist and rehabilitation specialist, University of Virginia Medical Center, Charlottesville, Va.; Jack W. Bowerman, MD, radiologist, of Johns Hopkins School of Medicine, Baltimore; Joseph S. Torg, MD, director of the Sports Medicine Center, University of Pennsylvania, Philadelphia; S. Harvard Kaufman, MD, psychiatrist, Seattle, Wash.

Further information on the conference is available from the Department of Environmental, Public and Occupational Health, American Medical Association, 535 N. Dearborn St., Chicago, Ill. 60610.

# Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

## Early Treatment Aids Cancer Cure

### Cancer Help Seen

A cancer occurs when abnormal cells begin a wild, unrestrained growth in some part of the body. They may spread by infiltrating adjacent tissue, by traveling through the circulatory and lymphatic systems to distant locations in the body, or by any combination of these. This growth and the spread of cancer cells will be fatal if not checked.

Your doctor treats cancer by surgery, by radiation to destroy the tumor, and special drug therapy. Often several of these treatments will be used. A few types of cancer, such as the leukemias, react quite well to hormones and newly discovered drugs.

The American Medical Association points out that one third of all cancers in the United States are being cured

today. Cancers are most readily curable if they can be treated before they spread from their original locations. To be cured, cancers must be found early and removed or destroyed before they have started to spread. Since two thirds of all cancers are on the surface of the body or close enough to the surface to be readily seen or felt, early detection often is possible.

Breast cancer is the leading cause of cancer deaths in American women. Lung cancer is a leading cause of death from cancer. Cancer of the larynx has persistent hoarseness as an early sign. Colon and rectal cancer will occur in more than 100,000 American men and women each year, and is the second highest cause of cancer deaths among women.

Cancers are curable if found and treated promptly. Early detection is largely the individual's own responsibility. It depends on an active interest in one's own health and a willingness to let the physician judge the importance of a danger signal.



September, 1979  
Frank Chappell  
Science News Editor  
AMA



ROCHE

# For recurrent attacks of urinary tract infection in women

## Bactrim™ DS Double Strength Tablets

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

### Just one tablet b.i.d. for 10 to 14 days



- Action at urinary/vaginal/lower bowel sites helps eliminate reservoirs of infecting organisms
- Distinctive antibacterial action plus wide spectrum helps eradicate recurrent UTI
- Low incidence of bacterial resistance in community practice

- Convenient *b.i.d.* dosage provides day-and-night antibacterial control
- Contraindicated during pregnancy and the nursing period. During therapy, maintain adequate fluid intake; perform CBC's and urinalyses with microscopic examination.

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications and Usage:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. Note: The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

**Also for the treatment of documented *Pneumocystis carinii* pneumonitis.** To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

The recommended quantitative disc susceptibility method (*Federal Register*, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers; infants less than two months of age.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache,

peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for infants less than two months of age.

**Urinary Tract Infections:** Usual adult dosage—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

Recommended dosage for children—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. A guide follows:

Children two months of age or older

Weight		Dose—every 12 hours	
lbs	kgs	Teaspoonfuls	Tablets
20	9	1 teasp. (5 ml)	½ tablet
40	18	2 teasp. (10 ml)	1 tablet
60	27	3 teasp. (15 ml)	1½ tablets
80	36	4 teasp. (20 ml)	2 tablets or 1 DS tablet

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	½ the usual regimen
Below 15	Use not recommended

***Pneumocystis carinii* pneumonitis:** Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100; Tel-E-Dose® packages of 100 Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole, fruit-licorice flavored—bottles of 16 oz (1 pint).

ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

Please see back cover.

Her next attack of cystitis may require

# the Bactrim 3-system counterattack



ROCHE

Bactrim has shown high clinical effectiveness in recurrent cystitis as a result of its wide spectrum and distinctive antimicrobial action in the urinary, vaginal and lower intestinal tracts.

The probability of recurrent urinary tract infection appears to be enhanced by the establishment of large numbers of *E. coli* or other urinary pathogens on the vaginal introitus. The trimethoprim component of

Bactrim diffuses into vaginal fluid in effective concentrations, thus combating migration of pathogens into the urethra.

Studies have shown that Bactrim acts against *Enterobacteriaceae* in the bowel without the emergence of resistant organisms. Thus, Bactrim reduces the risk of intestinal colonization by fecal uropathogens. It has no significant effect on other normal, necessary intestinal flora.

## Bactrim fights uropathogens in the urinary tract/vaginal tract/lower intestinal tract

Please see reverse side for summary of product information.



DISPLAY  
SHELVES



# BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

## CONTENIDO

LONG TERM PHYSIOLOGICAL CHANGES IN NORMAL IRRADIATED LUNGS

AN AMPLITUDE OF ACCOMMODATION CURVE FOR PUERTO RICO

EDITORIAL: UN RIESGO CALCULADO

PROGRAMA CIENTIFICO - ASAMBLEA ANUAL

CENTRO DE CONVENCIONES - CONDADO

NOVIEMBRE 6-10, 1979

ABSTRACTOS DE LITERATURA MEDICA

CURSOS - NOTICIAS

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NUM. 8

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# A character all its own.



Valium (diazepam/Roche)  
is a benzodiazepine with a  
character all its own.

Pharmacologically, it is a potent skeletal muscle relaxant and anticonvulsant (in adjunctive use), as well as an antianxiety agent. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

**Valium<sup>®</sup> <sup>IV</sup>**  
**diazepam/Roche**  
2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

**Dosage:** Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

**Supplied:** Valium<sup>®</sup> (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose<sup>®</sup> packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.



Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110



# The heart of the matter in hypertension is the kidney

The kidney—not the heart—is the key to long-term arterial pressure control. Diuretics help the kidney excrete sodium, reduce fluid volume and lower blood pressure.

No diuretic blocks sodium retention longer than Hygroton.

In mild hypertension low-dose Hygroton 25 mg. An effective, conservative therapy.

## In mild hypertension

Low-dose

# Hygroton<sup>®</sup> 25 mg. one a day

(chlorthalidone USP)

## Gets to the heart of the matter...simply

### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema.

**Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

**Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. There is a possibility of exacerbation or activation of systemic lupus erythematosus with thiazides, which are related to chlorthalidone. This has not been reported with chlorthalidone. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

**Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous

patients in hot weather. Hyperurcemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance.

**Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn.

**Usual Dose:** One tablet daily.

**How Supplied:** Tablets—100 mg. (white, scored), 50 mg. (aqua) and 25 mg. (peach) in bottles of 100 and 1000; unit-dose blister packs, boxes of 100 (10 x 10 strips). Also, 100 mg. and 50 mg. in PAKs of 28 tablets, boxes of 5.

**USV  
LABORATORIES**

**USV Laboratories Inc.  
Manati, P.R. 00701**

**In pediatric infections**

# **Septra<sup>®</sup>**

Each teaspoonful (5 ml) contains:  
40 mg trimethoprim and 200 mg sulfamethoxazole

## **Suspension B.I.D.**

**Acute  
Otitis  
Media**



## **where the action is.**



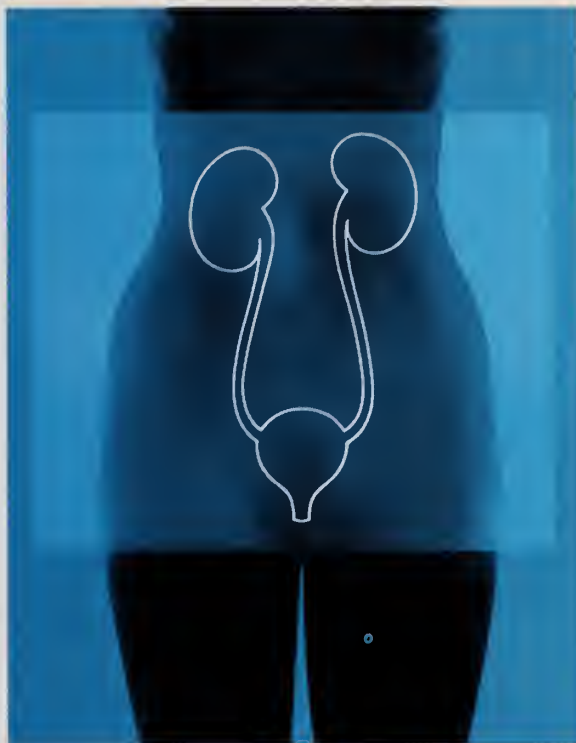
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## In acute otitis media

Septra Suspension provides effective antibacterial action against susceptible strains of H influenzae and S pneumoniae (D pneumoniae), the pathogens most likely to cause acute otitis media in children.

Septra Suspension is useful in many patients, but especially in those with penicillin allergy or with infections caused by ampicillin-resistant H influenzae. Limited clinical data are presently available on the effectiveness of treatment of acute otitis media with Septra when the infection is due to H influenzae resistant to ampicillin. However, in vitro data is highly favorable; when over 200 strains of ampicillin-resistant H influenzae were tested, all proved susceptible to TMP/SMX.\*

And unlike most other antibacterials for the treatment of acute otitis media, Septra Suspension is administered on a convenient b.i.d. dosage schedule. The cherry-flavored suspension is well accepted by children.



## In recurrent urinary tract infections

Septra Suspension provides effective antibacterial action in urine and blood against susceptible strains of E coli, Klebsiella-Enterobacter and Proteus. Whether the infection centers in the kidneys or bladder, Septra Suspension maintains effective levels at the site of the infection with just two doses a day.

Adequate fluid intake should be maintained and frequent urinalyses with careful microscopic examination performed during Septra therapy. Septra is contraindicated in infants under two months of age.

\*In vitro data do not necessarily correlate with clinical results. Data on file, Burroughs Wellcome Co.  
NOTE: Septra should not be used in the treatment of streptococcal pharyngitis.

Please see prescribing information on next page.



Wellcome

**Burroughs Wellcome Co.**  
Research Triangle Park  
North Carolina 27709

# Septra® Suspension B.I.D.

Each teaspoonful (5 ml) contains: 40 mg trimethoprim and 200 mg sulfamethoxazole

# Septra® DS B.I.D.

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

## Septra® DS Tablets Double Strength

## Septra® Tablets

## Septra® Suspension

### INDICATIONS AND USAGE:

**URINARY TRACT INFECTIONS:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

**NOTE:** Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

**ACUTE OTITIS MEDIA:** For the treatment of acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to *Haemophilus influenzae* resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.

**SHIGELLOSIS:** For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

**PNEUMOCYSTIS CARINII PNEUMONITIS:** For the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

**CONTRAINDICATIONS:** Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

**WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.**

Clinical studies have documented that patients with Group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

**PRECAUTIONS:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

**ADVERSE REACTIONS:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood Dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic Reactions:* Erythema multiforme, Stevens-Johnson

syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal Reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *C.N.S. Reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous Reactions:* Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L. E. phenomenon have occurred.

Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

**DOSAGE AND ADMINISTRATION:** Not recommended for use in infants less than two months of age.

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:**

**Adults:** The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

**Children:** The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose—every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 ( 5 ml)	1/2
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1 1/2
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

### PNEUMOCYSTIS CARINII PNEUMONITIS:

The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose—every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 ( 5 ml)	1/2
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1 1/2
70	32	4 (20 ml)	2 (or 1 DS tablet)

**HOW SUPPLIED:** TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

**ORAL SUSPENSION,** containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.



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## ASOCIACION MEDICA DE PUERTORICO

VOLUMEN 71

I N D I C E

NUMBER 8

- \* Long Term Physiological Changes in Normal Irradiated Lungs ..... 283  
*A. E. Lanaro, MD and A. Elías de Alonso, MD*

In this article Lanaro and Elías de Alonso present the results of lung perfusion studies in 21 patients receiving radiotherapy to the thorax for malignant diseases without lung involvement. At a time when radiotherapists and internists are concerned about the effects of irradiation in normal lung tissue, this article provides useful information for all of us involved in the long term follow-up of patients with malignant lesions.

Decreased perfusion was observed in 20 of 21 patients studied. This usually occurs either during therapy or within the first 3 months of therapy. Most important, according to the author, the perfusion defects may persist for years.

- \* An Amplitude of Accommodation Curve for Puerto Rico ..... 291  
*Manuel N. Miranda, MD*

The amplitude of accommodation was measured by Dr. Miranda in 1,253 patients aged 10 to 65 years. His study showed that the amplitude of accommodation varies for each age group, for different geographical regions and tends to decrease faster in countries near the equator.

Dr. Miranda compares his findings to those published in other studies. Significant differences were found. These differences appear to explain the earlier onset of presbyopia in India and Puerto Rico than in New York and England. This is both a pertinent and well timed study that should be of great interest to our readers.

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## LONG TERM PHYSIOLOGICAL CHANGES IN NORMAL IRRADIATED LUNGS

A. E. Lanaro, MD and A. Elías de Alonso, MD

**Summary:** Twenty-one patients with normal lungs, receiving irradiation incidental to therapy for malignant disease, were studied before irradiation, during irradiation and up to three months after therapy. They were also followed yearly for periods ranging from one to four years. Lung perfusion by radioisotope techniques was performed in all patients before irradiation therapy and serially thereafter. In eight patients, studies of total pulmonary function were performed before therapy and at similar intervals. Sixteen patients had carcinoma of the breast, three had Hodgkin's disease, one had sarcoma of the stomach and one had histiocytic lymphoma. Decreased perfusion in the irradiated area occurred in 20 of 21 patients. This occurred early (during therapy or up to 3 months after) in 16 of the patients. These early changes disappeared by the end of one year in only 1 of the 16 patients. In 14 patients of the whole group, or 67 percent, the impaired perfusion persisted throughout the period of study. Of the 8 patients who had total pulmonary function studies, none had early changes which can be attributed to irradiation and the two patients who developed changes late in the observation period, at 2 and 3 1/2 years respectively, had evidence of me-

tastatic complications. It is suggested that pulmonary function impairment associated with irradiation is best demonstrated by studies of perfusion. The decreased perfusion usually occurs either during therapy or within the first 3 months after therapy. In the majority of the patients affected, the impairment persists for years, but reversibility of the abnormality can be demonstrated in some cases.

**Resumen:** Veintiún pacientes con pulmones normales, irradiados incidentalmente mientras recibían terapia de irradiación para tumores malignos extrapulmonares, fueron estudiados antes de la terapia, durante la terapia, por los primeros tres meses y seguidos anualmente por períodos entre uno y cuatro años. Estos estudios incluyeron gamagramas de perfusión pulmonar en todos los casos. Se les hizo estudios de la función pulmonar a 8 pacientes. Los diagnósticos en los pacientes estudiados son como sigue: 16 casos de cáncer de la mama, 3 casos de enfermedad de Hodgkin, 1 sarcoma de estómago y 1 linfoma hitiocítico. Veinte de los 21 pacientes demostraron disminución de la perfusión en el área irradiada. Esto ocurrió temprano (hasta 3 meses) en 16 pacientes. Estos cambios tempranos desaparecieron al final de un año en solo 1 de los 16 pacientes. En 14 pacientes del total, o un 67 por ciento, la deficiencia en perfusión persistió a través de todo el período de observación. De los 8 pacientes a los cuales se les hizo estudios de la función pulmonar, ninguno

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*From the Nuclear Medicine Division, Center for Energy and Environment Research (former Puerto Rico Nuclear Center), University of Puerto Rico, and the Pulmonary Function Laboratory, University District Hospital, Puerto Rico Medical Center, University of Puerto Rico.*

tuvo cambios tempranos que pudieran atribuirse a la irradiación y los 2 casos que desarrollaron cambios tardíos, a los 2 y 3 1/2 años respectivamente, tenían evidencia de metástasis pulmonar. Se concluye que los cambios fisiológicos adversos secundarios a la irradiación pulmonar se pueden demostrar mejor por medio del gamagrama de perfusión. La disminución en la perfusión ocurre generalmente durante la terapia o dentro de los primeros 3 meses. En la mayor parte de los pacientes afectados, esta anomalía persiste por años pero se puede observar reversibilidad de la misma en algunos casos.

### Introduction

Radiotherapists and physicians in general have been concerned for years about the effects of irradiation on normal lung tissue. The histopathological picture of radiation pneumopathy and its correlation with the radiological changes are well documented (1, 2). As to the early physiological alterations, these have been studied rather extensively in animals (3-6). Early effects (up to 3 months after therapy) on the normal human lung have been reported by several investigators including the present authors (7-9). This report presents the results obtained in 21 patients followed, for one to four years. Most studies of late physiological effects of irradiation on the normal human lung have been performed in groups of patients which included cases with lung involvement due to the malignancy being treated. The present study was undertaken to determine the long term effects of radiation therapy on the normal lung and the duration and reversibility of these changes.

### Material and Methods

Twenty one patients were studied, who were

receiving radiotherapy to the thorax for malignant disease not involving the lungs. The group included 16 cases of carcinoma of the breast, 3 cases of Hodgkin's disease, 1 reticulum cell sarcoma of the stomach and 1 histiocytic lymphoma. Radiation dosage varied from 4000 to 5000 rads (except for the case of sarcoma of stomach who had 3000 rads). The average dosage was 4600 rads. The extent of the irradiated field varied between 100 - 300 cm<sup>2</sup>. The regions irradiated are outlined in Table I. The duration of radiotherapy was 5 weeks. Treatment was administered from a source of <sup>60</sup>Co (El Dorado 8000 Ci).

Absence of pulmonary disease and of pulmonary involvement by the malignant process was established by thorough clinical evaluation, chest X-rays, and perfusion scan. Ages varied from 11 to 61 years with an average age of 42.5 years. Perfusion scans with macroaggregates of albumin <sup>99</sup>Tc were performed in a linear scanner or a Gamma Camera. Studies were done before radiotherapy and subsequently at mid therapy, at the end of therapy, after 1 month, 3 months, 1 year, and yearly up to 4 years. All patients of breast carcinoma and the patients with sarcoma of the stomach had surgery about one month before baseline studies. Periods of follow up are shown in Table II.

Total pulmonary function studies were performed before radiotherapy and at the same intervals during and after treatment in 8 of the 21 patients. These studies included all lung volumes (Vital Capacity, Total Lung Capacity, Expiratory Reserve Volume, Inspiratory Capacity, Functional Residual Capacity, and Residual Volume) expiratory flow rates and steady state diffusion capacity. Arterial blood gases were done in all patients before therapy and in some patients subsequently. Patient No. 3 had unexplained diffusion impairment before therapy which persisted unchanged throughout the whole period of evaluation.

### Results

Of the 21 patients studied, perfusion impairment was seen within the first three months after therapy in 16 patients. Long term effects were evaluated at periods ranging from 1 to 4 years. Three patients showed impairment at the one year follow up but none of these had shown up at 1 and 3 months, so it is quite

TABLE I  
Distribution of the Cases by Treatment Region

---

<i>Supraclavicular, costal wall (tangential) and axillary</i>	-7
<i>Supraclavicular, axillary and internal mammary</i>	-7
<i>Infraclavicular and axillary</i>	-1
<i>Left hypochondrium</i>	-1
<i>Mediastinum</i>	-2
<i>Supraclavicular, axillary and mediastinum</i>	-1
<i>Supraclavicular and costal wall (tangential)</i>	-1
<i>Left clavicular</i>	-1

---

21

---

possible that the perfusion changes observed at one year had been present earlier. Only one patient, case No. 19, showed no impairment of perfusion at anytime. This was a case of histiocytic lymphoma who was seen regularly at all periods of observation up to 2 years after irradiation and was still doing well when last seen.

The impairment in perfusion in the area exposed persisted for the periods of follow up concerned in 14 of the twenty patients who developed these changes. The stages at which these changes cleared are shown in Table II. A complete picture of onset of abnormality in perfusion and of clearing of abnormality when this occurred is shown in the same table. In 9 patients impaired perfusion was noted in areas not exposed to irradiation.

As shown in Table II changes in perfusion appeared early and persisted in the ma-

jority of cases. At the end of one year, only one patient had the impairment cleared. Late disappearance of the perfusion abnormality was observed in 5 additional patients, at 2, 3, and 4 years.

Of the eight patients who had complete pulmonary function studies only two had significant changes and these occurred late. Patient No. 2 had hypoxemia and decreased Total Lung Capacity, Vital Capacity and Inspiratory Capacity, decreased expiratory flow rates and hypoxemia at 3 1/3 years after therapy. She had normal function at all previous periods of observation. This was a case of mammary carcinoma who had bilateral pleural effusions at the time. The other patient, No. 4, had decreased TLC, VC and IC, impaired diffusion capacity ( $DL_{CO_{SS}}$ ) and impaired expiratory flow rates at the 2 year observation period. She too, was a case of breast carcino-



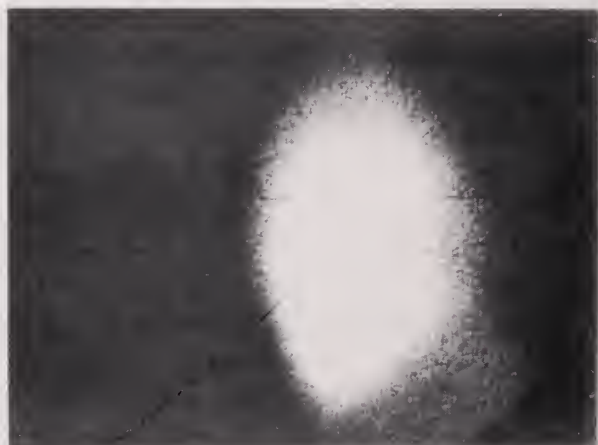


Figure 1: Lung Scan. Patient with Hodgkin's Disease. Irradiation of Mediastinum. Enlarged Mediastinum space.

ma and shortly after was shown to have pleuro pulmonary complications with bilateral effusions.

### Discussion

The direct irradiation of the chest for malignancy produces functional impairment in the human lung. This has been described

by several authors. Emergil and Heinemann reported a progressive decrease in lung volumes, hypoxemia, and reduced diffusing capacity (10). Teates and Cooper (11) followed 16 patients irradiated for carcinoma of the lung and other malignancies for up to 40 months and found in only two of these significant reduction in Vital Capacity and Maximum Breathing Capacity. The effects of mantle irradiation for Hodgkin's disease was studied

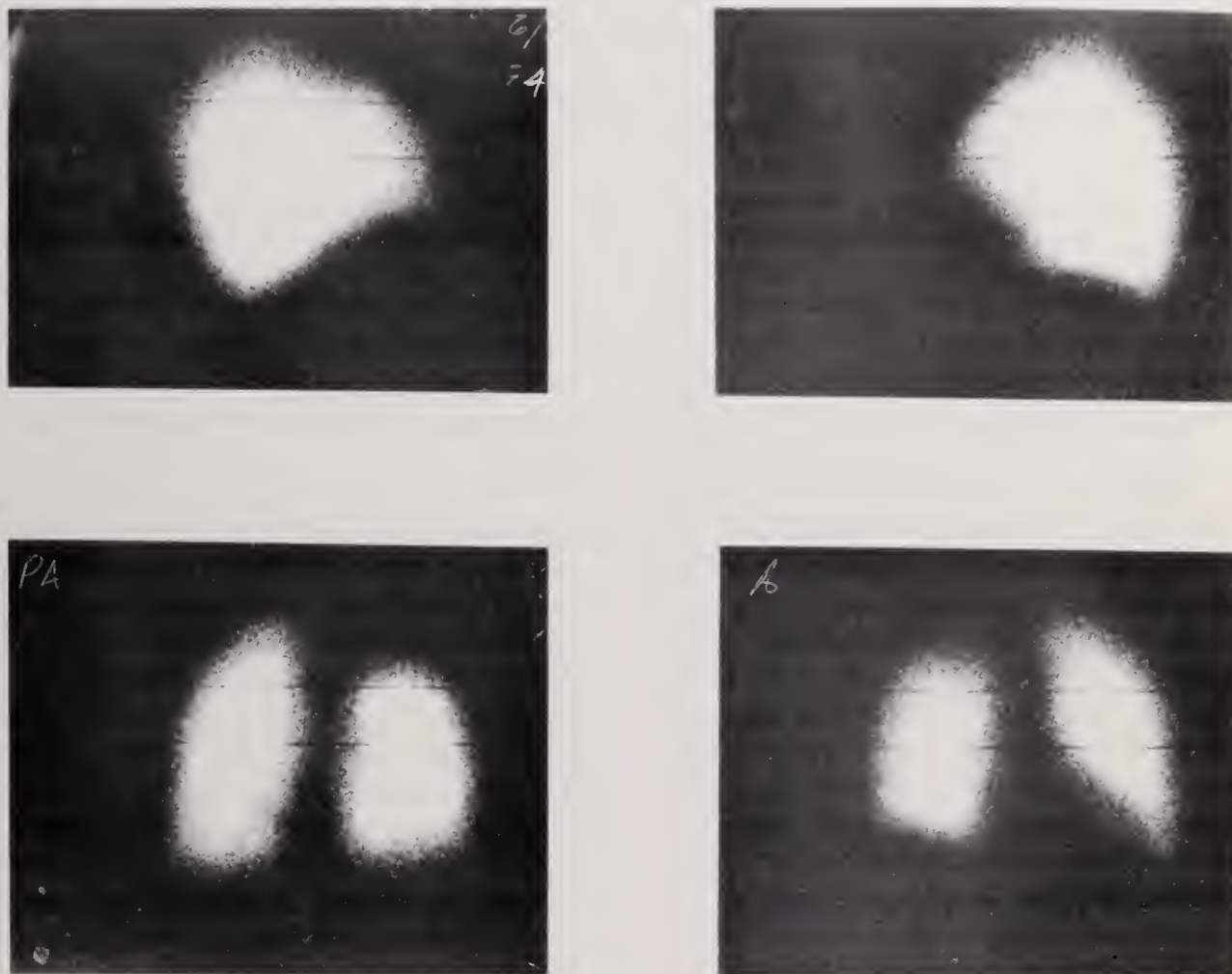


Figure 2: Lung Scan. Patient with Ca of Breast (Right). After irradiation, hypoperfusion of right apex.

by Lakich et al (12) who found that lung volumes are maximally affected at 9 months, returning to normal at 24 months. Evans and his group, however, in the same type of patients, reported maximal effects at 4 -6 months which subsided at eight months (13).

Modern methods of irradiation for mammary carcinoma and other malignancies utilize tangential chest wall exposure in order to decrease exposure of lung tissue to irradiation.

Adverse effects are thus minimized when the usual therapeutic dosages are used. Long term effects in the normal human lung were reported recently by Prato and co-workers (14) who suggest that changes at 60 days after irradiation are predictive of long term effects. They conclude that blood flow measurements afford the earliest and greatest change. In the present study, using the same therapeutic approach, a group of 21 patients were studied at intervals

TABLE II

## Abnormalities in Perfusion and Regions Involved in Relation to Periods of Follow Up

Patient No.	Diagnosis	Before Radio-therapy	Mid Ther-apy	End	1 mo.	3 mos.	1 yr.	2 yrs.	3 yrs.	4 yrs.
1	Carcinoma right breast	N	N	N			RA	RA		
2	Carcinoma right breast	N		N*	N*	N*	RA	RA	RA	
3	Carcinoma right breast	N	N*	RA	RA	RA	RA			
4	Carcinoma right breast	N	N	N	RA	RA	RA	RA	RA	
5	Carcinoma right breast	N	N	N	RA		RA	RA	RA	N
6	Carcinoma right breast	N		N	RA	RA	RA	RA	RA	RA
7	Hodgkin's	N	N	N		MB	N			
8	Hodgkin's	N		RA	RA & LA		RA & LA		N	
9	Carcinoma left breast	N	N	N	LA	LA	LL	N*	N	N
10	Carcinoma right breast	N		RA	RA	RA	RA			
11	Carcinoma left breast	N*	N	LA	LA	LA		RA & LA	RA	& LA
12	Carcinoma right breast	N	N	N		RA	RA			
13	Carcinoma right breast	N	N		RA	RA	RA & LA	RA		
14	Carcinoma left breast	N		N	LA	LA	LA			
15	Carcinoma left breast	N	N	N	N	LA	N	LA		
16	Carcinoma right breast	N*	RA	N*	N*	RA	RA			
17	Carcinoma left breast	N	N	N			LA	LA	N*	
18	Sarcoma of stomach	N		N			LB	N*		
19	Histiocytic lymphoma	N		N		N	N	N		
20	Hodgkin's	N		LL			N		MB	
21	Carcinoma right breast	N	N	N	N*	RA	RA	RA	RA	RA

Localization of perfusion impairment in areas exposed to irradiation.

RA = right apex LA = left apex LL = left lung LB = left base MB = medial borders of lung

N = normal perfusion scan N\* = normal in area irradiated, but showing abnormality elsewhere

up to 4 years. The early changes in lung perfusion which were observed extend the author's experience in a similar group of patients reported earlier (9) some of which are included in the present study. In that group of patients followed up to 3 months it was found that 22

out of 32 patients had impaired perfusion of the area exposed during therapy while the eight patients who had pulmonary function tests done, did not show any significant alteration in lung volumes, expiratory flow rates or diffusion capacity. In the present study, 16



of 21 patients showed decreased blood flow, as determined by radioisotope techniques, in the area exposed by the third month after therapy. No significant changes in the total lung function were seen at that stage in any of the 8 patients who had these studies done.

As to the late physiological changes, in 14 of the 21 patients perfusion impairment persisted for one year or longer. In two of three patients in whom changes were observed at 1 year, but were not seen at 1 and 3 months (see results), persisted up to 2 and 3 years respectively. It is apparent that in most cases, the late changes in perfusion represent a persistence of changes observed at an early stage (up to 3 months after radiotherapy). Meyer, in his study based on X-Ray findings (15), concludes that at 6 months after therapy the lesions stabilize and that lesions observed after that time are highly suggestive of recurrent tumor.

Reversibility of perfusion impairment in the area exposed was observed in 6 of the 21 patients, occurring as late as the 4th year in one case (see Table II). Some reversibility shown as improvement is reported by Prato and co-workers (14).

Abnormalities in perfusion in areas of lung not exposed to radiotherapy occurring within the first three months were observed in 3 patients. These changes were reversible and could represent a manifestation of hyperimmune response, as has been suggested by some authors (2).

The late changes in total pulmonary function which were observed in 2 of the eight patients were explained by pulmonary metastasis (see results).

### Conclusions

1. Most patients with normal lungs subjected

to irradiation, even with optimal irradiation techniques, will have a radiation reaction which is irreversible in about 2/3 of those affected. In most cases the reaction is mild and does not produce symptoms.

2. Study of pulmonary perfusion by radioisotope techniques is a sensitive index of functional impairment in such cases.
3. Radiation pneumopathy will usually occur during therapy or up to 3 months after therapy.
4. Later changes observed, usually represent persistence of changes that have occurred within the first three months after radiation therapy. New changes occurring after one year should be suspected of metastatic involvement.
5. Studies of total pulmonary function by conventional pulmonary function studies are not sensitive to determine the effect of irradiation on the normal lung. This is probably because, with modern methods of irradiation, the effect is localized and not severe enough to produce significant changes in total pulmonary function.
6. Perfusion changes sometimes occur in areas of lung not exposed to irradiation.

### Acknowledgments

We want to express our gratitude to Dr. Antonio Bosch and Dr. René Dietrich, who collaborated in the early part of this work, and to Miss Ilvia Millán, Mrs. Carmen C. de Villodas and Mrs. Luz S. Emanuelli for their technical assistance. We also are indebted to the staff of the Radiation Oncology Division of the University of Puerto Rico, School of Medicine, who referred the patients.

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# Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

## Rheumatic Fever Hits Young Hearts

### Fever Hits Heart

Rheumatic fever accounts for much of the heart disease found in children and young adults.

Rheumatic fever usually occurs between the ages of 5 and 15, although adults can have it. It may affect any part of the body temporarily, but damage to the heart, which can be long lasting, is the greatest danger.

Rheumatic heart disease results from the scarring of the heart muscle and valves by rheumatic fever. This may interfere with the vital work of the heart. Many patients recover without permanent injury to the heart valves, but the disease has a

way of repeating itself and each attack renews the chances of heart damage.

Rheumatic fever is preceded by a streptococcal infection such as strep throat, scarlet fever or a strep ear infection. It can be prevented by treating the strep infection promptly and thoroughly with antibiotics.

Because persons who have had rheumatic fever are susceptible rather than immune to repeat attacks, long-term preventive treatment is often prescribed for them. Regular doses of penicillin, under the direction of a physician, can prevent further strep infections and thus ward off subsequent attacks of rheumatic fever.

You can protect your child against rheumatic fever by consulting your doctor if the child develops a sudden, severe sore throat, or if he or she has been exposed to someone with scarlet fever or another strep infection.



October, 1979  
Frank Chappell  
Science News Editor  
AMA



# The Maker

## Examining a Few Myths About Prescribing.

Increasing pressure is being put on the practicing physician to prescribe drugs generically. You are told that brand-name products are universally "expensive" and generic versions are relatively "cheap." To make this case, the most extreme (rather than typical) price differentials are cited. Thus, consumers are led to believe that such differentials are commonplace. Even your knowledge and your motives as a physician are questioned.

Understandably, these views have created myths. We think it's time to examine them in the light of all the facts and ramifications.



*MYTH: There are no differences in quality and performance between brand-name products and their generic counterparts. The corollary is that there are no differences among products made by high-technology, quality-conscious, research-based companies and those made by commodity-type suppliers.*

**FACT: The Food and Drug Administration does a good job in monitoring a generally excellent drug supply. Still, it has nowhere near the resources to guarantee the quality and bioavailability of all marketed products at any given time. Just a few months ago, for example, it noted that batches of tetracycline HCl capsules which met official monograph requirements were**

not bioequivalent to a reference product. As you know, there is substantial literature on this subject affecting many drugs, including such antibiotics as tetracycline and erythromycin. The record of drug recalls and court actions affirms strongly that there are differences among pharmaceutical companies and their products. Research-intensive companies have far better records than those that do no research and may practice minimum quality assurance.

*MYTH: Industry favors only "expensive" brand names and denigrates all generics.*

**FACT: PMA companies make 90 to 95 percent of the drug supply, including, therefore, most of the generics. Drug nomenclature is not the important point; it's the competence of the manufacturer and the integrity of the product that count.**

# Matters.

**MYTH:** Generic options almost always exist.

**FACT:** About 55 percent of prescription drug expenditure is for single-source drugs. This means, of course, that for only 45 percent of such expenditure, is a generic prescribing option available.

**MYTH:** Generic prescriptions are filled with expensive generics, thus saving consumers large sums of money.

**FACT:** Market data show that you invariably prescribe—and pharmacists dispense—both brand and generically labeled products from known and trusted sources, in the best interest of patients. In most cases the patient receives a proven brand product. Savings from voluntary or mandated generic prescribing are grossly exaggerated.

**MYTH:** Drugs account for a major portion of the rise in health care costs.

**FACT:** Drugs represent a very small part of such costs. The amount of the health care dollar spent for prescription drugs was about 12 cents in 1967; today it is about 8 cents. And you as a physician are most conscious of how drug therapy can cut hospitalization, avert surgery, reduce office visits and keep patients on the job.

**MYTH:** Government intrusions into the marketplace will save tax money.

**FACT:** Government schemes always cost the taxpayer something, and the costs often exceed the benefits. Certainly, any federal “help,” such as lists of wholesale drug prices sent to all physicians and pharmacists, will be no exception. Just think of the expense of keeping them current! Moreover, wholesale prices are poor guides to actual transaction prices and even worse guides to retail prices.

## The PMA Position

We believe your freedom to prescribe, either by generic or brand name, should be totally unabridged. Otherwise, your prescribing prerogatives and your relationships with patients will be seriously impaired.

## The maker does matter

After the myths about price and equivalency have been shattered, one fact stands out more clearly than ever: *The maker does matter.* As always, your best guide to drug therapy for your patients is to select products—both brands and generics—from manufacturers with credentials and performance records you have come to respect.



Pharmaceutical Manufacturers Association  
1155 Fifteenth Street, N.W.  
Washington, D.C. 20005



## LISTA DE ANUNCIANTES

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Septra

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Vioform-HC

### MEAD JOHNSON PHARM. DIV.

Colace  
Quibron

### MERRELL-NATIONAL

Bentyl  
Tenuate

### NORWICH INTERNATIONAL

Macrochantin

### PHARM. MFG.

Institutional

### ROCHE LAB.

Librium  
Valium

### RORER INTERNATIONAL

Maalox Plus

### S. L. COMPANY

Lact-Aid

### SMITH, KLINE & FRENCH

Tagamet

### U.S.V. PHARM.

Hygroton 25

### THE UPJOHN COMPANY

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## Tenuate®

(diethylpropion hydrochloride NF)

## Tenuate Dospan®

(diethylpropion hydrochloride NF) controlled-release

### AVAILABLE ONLY ON PRESCRIPTION

#### Brief Summary

**INDICATION:** Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence:* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache; rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSAGE AND ADMINISTRATION:** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in midmorning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSAGE:** Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.

Cayey, Puerto Rico 00633

Direct Medical Inquiries to

MERRELL-NATIONAL LABORATORIES

Division of Richardson-Merrell Inc.

Cincinnati, Ohio 45215, U.S.A.

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# Merrell



**Overweight may not always be simple...  
complications can develop\*.  
Complicated or not...**

# **Tenuate<sup>®</sup> Dospan<sup>®</sup> <sup>IV</sup>** **(diethylpropion hydrochloride NF)** **75 mg. controlled-release tablets**

## **A useful short-term adjunct in an indicated weight loss program.**

Overweight patients in certain diagnostic categories often require strict appetite control and a successful program of weight reduction may tend to diminish the incidence or severity of the complications in some patients. Diethylpropion hydrochloride has been reported useful in such patients and while it is not suggested that Tenuate itself in any way reduces the complications of overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. **Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.**

## **In uncomplicated overweight.**

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

## **Clinical effectiveness.**

The anorectic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.<sup>1</sup> And the unique chemistry of Tenuate provides "...anorectic potency with minimal overt central nervous system or cardiovascular stimulation."<sup>2</sup> Compared with the amphetamines, diethylpropion has minimal potential for abuse.

**Tenuate—it makes sense.  
And it's responsible medicine.**



\*Studies have shown that obesity is associated with an increased incidence of hypertension, symptomatic heart disease, adult-onset diabetes, and other diseases.

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J-6999-4

April 1979

# AN AMPLITUDE OF ACCOMMODATION CURVE FOR PUERTO RICO

Manuel N. Miranda, MD

**Summary:** The amplitude of accommodation of 1,253 Puerto Ricans between the ages of 10 and 65 years were measured using the best possible subjective method. Results were compared with those found in other regions. An amplitude of accommodation curve was developed for Puerto Rico.

**Resumen:** Se midió la amplitud de acomodación de 1,253 puertorriqueños entre las edades de 10 a 65 años usando el mejor método subjetivo disponible. Los resultados fueron comparados con los encontrados en otras regiones. Se construyó una curva de amplitud de acomodación para Puerto Rico.

## Introduction

The eye cannot distinguish near (1) objects when it is adapted for far, nor distant objects when it is adapted for near. In order for the eye to see objects distinctly at dif-

ferent distances a change must be made, either in the position of the retina or in the refractive power of the dioptric system. Under physiologic conditions, the eye cannot change the position of the retina so in order to focus clearly near objects it must increase the power of the crystalline lens. The process by which the lens increases its power is known as accommodation.

The total accommodative power which an eye possess is represented by the difference between its refraction when at rest and the refraction when the maximum effort of accommodation is elicited. This is known as the amplitude of accommodation.

To give the correct prescription needed for persons with active accommodation, the amplitude of accommodation should be determined for each one. However, this is not always possible. An amplitude of accommodation curve helps in finding the adequate correction for most individuals.

Since Alexander Duane published in 1912 his findings for the normal values of the accommodation at all ages, (2) his amplitude of accommodation curve has served as reference almost universally. Other investigators have published curves (3-9) in the different regions of the world with values for any given age that differ between themselves and those of Duane. The variations have been attributed to several factors foremost among them are different methods used by each investigator and different races, climate and diet

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*From the Department of Ophthalmology, School of Medicine, University of Puerto Rico.*

*Presented as the Fourth Dr. Antonio Navas Memorial Lecture during the Tenth Annual Ophthalmology Convention of Puerto Rico in November 19, 1978, at the Dorado Beach Hotel, Dorado, Puerto Rico.*

*Request reprints to: Manuel N. Miranda, MD, GPO Box D, San Juan, Puerto Rico 00936.*



in different regions of the world.

It would seem, therefore, that there probably are differences in amplitudes in different countries, so, I decided to find out the normal values of accommodation for the age group of 10 to 65 years in Puerto Rico.

## Method

I measured the amplitude of accommodation in one thousand two hundred fifty three Puerto Ricans between the ages of 10 to 65 years.

The patient is given an exact distance refraction; monocular as well as binocular visual acuities are noted. One percent solution of Cyclopentolate is used on patients 10 to 42 years of age, and their amplitudes are measured at least one week later. One percent Tropicamide solution is used on patients with heavily pigmented irises in addition to Cyclopentolate.

Patients with monocular visual acuities less than 20/20, or with ocular pathology, tropias and anisometropias exceeding one diopter or that obviously do not try to make use of the full amount of their accommodation are excluded from the study.

The amplitude of accommodation is measured with a near visual acuity chart consisting of a paragraph of letter height .485 mm, printed black on a non glossy background. The illumination of the chart is 8 foot candles for all tests.

In case of emmetropic patients the chart is placed exactly 33.3 cm. from the corneas; the letter height of .485 mm then corresponds to a visual acuity of 20/20, and the required accommodation is 3.00 D.

To determine as accurate as possible the amplitude of accommodation, it is necessary to eliminate the effect which the location of ametropic corrections has on the required accommodation. This is accomplished as follows:

The distance correction, carefully centered, is placed in a refractor 14 mm from the corneas. The monocular test is made first, then the binocular test follows.

In case of a hyperopic correction, the chart is placed 1 cm. farther than 33.3 cm. for every diopter correction; or, when the correction is astigmatic, for every diopter of the spherical equivalent. In the bi-

nocular test, the average of the spherical equivalents is taken.

In case of a myopic correction, the procedure is the same with the exception that the chart is placed 1 cm. closer than 33.3 cm. for every diopter correction or its spherical equivalent.

Precise analysis of this method shows that in all cases the required accommodation for reading the chart is 3.00 D and that the effect on the required visual acuity is negligible.

Example: Suppose the patient's distance correction is

O.D. -2.00 - 1.00 x 90°;  
spherical equivalent: -2.50 D

O.S. -1.00 - 0.50 x 75°;  
spherical equivalent: -1.25 D

Average -1.87 D

Subsequently, the chart is placed 2.50 cm. closer when testing the right eye; 1.25 cm. closer when testing the left eye; and 1.87 cm. closer when making the binocular test.

After placing the near visual acuity chart at the calculated distance, the patient is asked to read loudly the paragraph of the smallest letters corresponding to a visual acuity of 20/20. Minus spheres are added, first in 0.50 D steps, and later in 0.25 D, until the text can no longer be read. During the test the target is moved 1 cm. closer for every diopter of minus power introduced. The amplitude of accommodation is then 3.00 plus the number of minus diopters added.

If the patient cannot read the smallest letters, he is presbyopic; plus spherical power is added to his distance correction first in 0.50 D steps, later in 0.25 D, until he can just barely decipher the text. His amplitude of accommodation is then 3.00 D minus the number of diopters added.

## Results

The test was performed in 1,253 patients 10 to 65 years old, 812 females and 441 males. Age and sex of the individual patient were

TABLE I

Mean Binocular Amplitude of Accommodation of 1,253 Puerto Rican  
 Patients: Ages 10 to 65 years

<i>Age Groups</i>	<i>Sex</i>	<i>No. of Cases</i>	<i>Mean</i>	<i>S.D.</i>
10-12	<i>F</i>	20	9.40	.710
	<i>M</i>	14	9.48	.787
	<i>Both</i>	34	9.43	.733
13-15	<i>F</i>	28	8.74	.595
	<i>M</i>	13	9.01	.649
	<i>Both</i>	41	8.83	.618
16-18	<i>F</i>	36	8.61	.658
	<i>M</i>	19	8.76	.792
	<i>Both</i>	55	8.66	.703
19-21	<i>F</i>	28	8.09	.628
	<i>M</i>	14	8.23	.653
	<i>Both</i>	42	8.14	.632
22-24	<i>F</i>	22	7.92	.810
	<i>M</i>	13	7.79	.967
	<i>Both</i>	35	7.87	.860
25-27	<i>F</i>	19	7.41	.465
	<i>M</i>	10	6.88	.580
	<i>Both</i>	29	7.22	.560
28-30	<i>F</i>	20	6.62	.723
	<i>M</i>	25	6.32	.691
	<i>Both</i>	45	6.45	.713
30-32	<i>F</i>	25	6.06	.910
	<i>M</i>	32	6.02	.789
	<i>Both</i>	57	6.05	.836
33-35	<i>F</i>	38	5.08	.966
	<i>M</i>	29	5.65	.765
	<i>Both</i>	67	5.33	.923

36-38	<i>F</i>	34	4.22	.998
	<i>M</i>	14	4.49	.980
	<i>Both</i>	48	4.30	.937
39-41	<i>F</i>	73	2.35	.599
	<i>M</i>	23	2.45	.717
	<i>Both</i>	96	2.38	.627
42-44	<i>F</i>	69	1.69	.397
	<i>M</i>	31	1.94	.453
	<i>Both</i>	100	1.77	.430
45-47	<i>F</i>	86	1.39	.272
	<i>M</i>	42	1.46	.348
	<i>Both</i>	128	1.41	.300
48-50	<i>F</i>	69	1.26	.246
	<i>M</i>	57	1.40	.474
	<i>Both</i>	126	1.32	.372
51-53	<i>F</i>	67	1.26	.233
	<i>M</i>	37	1.22	.241
	<i>Both</i>	104	1.25	.236
54-56	<i>F</i>	72	1.17	.220
	<i>M</i>	28	1.23	.225
	<i>Both</i>	100	1.19	.222
57-59	<i>F</i>	40	1.17	.237
	<i>M</i>	22	1.17	.209
	<i>Both</i>	62	1.17	.226
60-62	<i>F</i>	38	1.10	.197
	<i>M</i>	15	1.13	.208
	<i>Both</i>	53	1.11	.199
63-65	<i>F</i>	38	1.04	.169
	<i>M</i>	21	1.17	.183
	<i>Both</i>	59	1.08	.183

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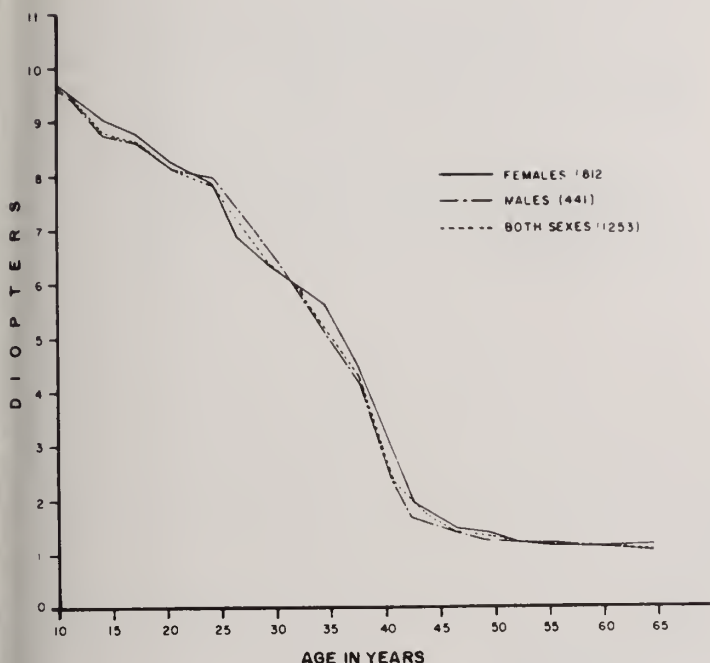


Figure 1: Mean binocular amplitude of accommodation of 1253 Puerto Rican patients: ages 10 to 65 years.

noted, and three groups were formed, females, males and both sexes.

Table I shows the mean binocular amplitudes of accommodation and standard deviation of the three groups. The number of patients studied in each group is also shown.

Figure 1 presents these results in graphic form. The findings for all groups differ very little, as the curves shown in the figure demonstrate.

#### Comment

The amplitude of accommodation is about the same for each age group both for females and males. Sex does not seem to affect the amplitude for equivalent ages.

Figure 2 shows the general characteristics of the curve for both sexes together; there is a drop of the amplitude of accommodation of about 1.25 diopters from 10 to 20 years; 1.75 D from 20 to 30 years, 3.75 D from 30 to 40 years, 1 D from 40 to 45 years, and a flattening of the curve from 45 to 65 years. It reveals that presbyopia begins in Puerto Rico between 38 and 39 years of age if we accept as a good criterion that presbyopia exists when amplitudes are below 3.75 D. A patient with an amplitude of 3.75 D can still read at 40 cm. (16 in.), the average reading distance, with 1/3 his amplitude in reserve, most likely the minimum reserve necessary for comfortable reading for long periods of time.

Figure 3 compares my findings with those of Duane, Turner (10) and Rambo (11).

Duane carried out his study in New York and published his findings in 1912; Turner, in England and published them in 1958; and Ram-

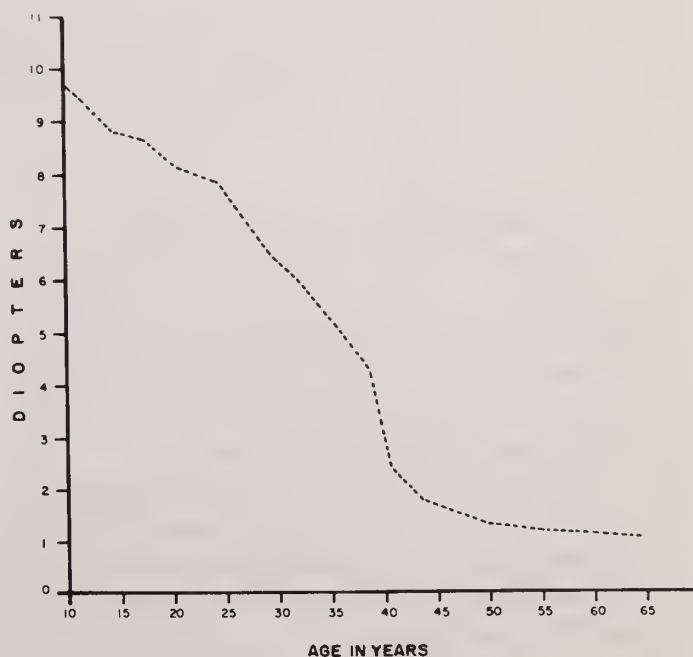


Figure 2: Mean binocular amplitude of accommodation of 1253 Puerto Rican patients, both sexes, 10 to 65 years.

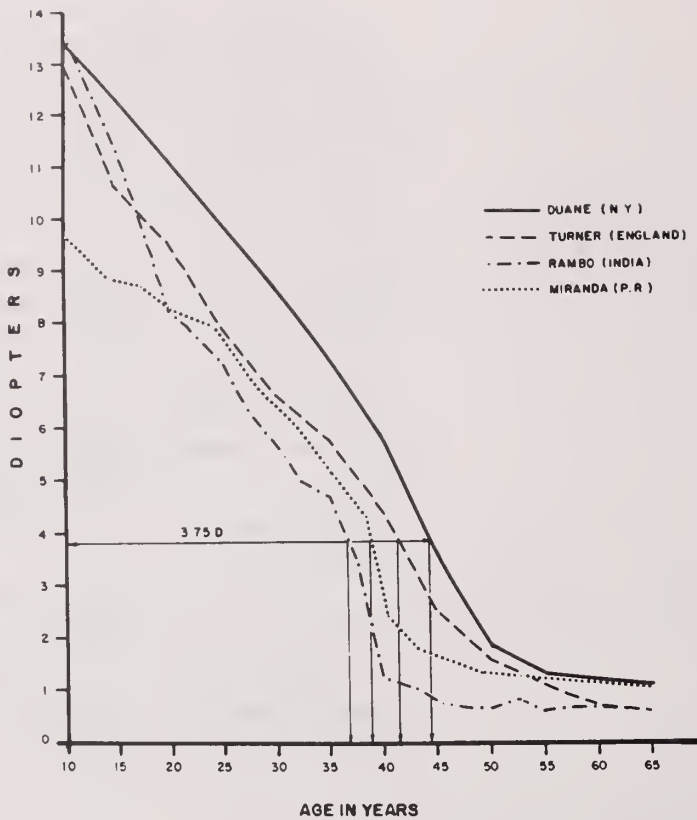


Figure 3: Mean accommodation in diopters in New York, England, India, Puerto Rico by year of age, from 10 to 65 years.

bo, in India and published them in 1957.

There is more or less a gradual drop in the amplitude of accommodation (A. A.) of the curves of Duane and Turner for ages between 10 and 65 years while there is a sharp drop of the A. A. in Rambo's (4.47 D) and mine (3.75 D) for ages between 30 and 40 years.

The rate of decrease of the amplitude of accommodation is faster in the curves of Rambo and mine; thus, explaining the earlier onset of presbyopia in India and Puerto Rico than in New York and England.

### Conclusion

This study shows that the amplitude of

accommodation varies for each age group for different geographical regions and that its rate of decrease tends to be faster in countries nearer to the Equator. To calculate the average amplitude of accommodation more accurately, an amplitude of accommodation curve should be developed for each region.

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## UN RIESGO CALCULADO

*Que el acto quirúrgico constituye un insulto al aparato respiratorio está muy claramente ilustrado cuando se examinan las causas principales de admisión a las unidades de cuidado intensivo respiratorio o aquellas unidades de cuidado intensivo general en ausencia de la primera; en ambas la principal indicación de admisión sigue siendo el cuidado post-operatorio. Queda bien implícito de lo arriba indicado que los efectos generales de cualquier tipo de cirugía sobre los pacientes con aparatos respiratorios normales y con enfermedad pulmonar pre-operatoria deben ser considerados con antelación al acto quirúrgico.*

*Todos los que estamos envueltos en el cuidado médico, y en especial los médicos responsables del futuro paciente quirúrgico debemos hacernos varias preguntas....*

*¿Podemos predecir preoperatoriamente los efectos que sobre el paciente ejercerá la cirugía?*

*¿Pueden ocurrir complicaciones pulmonares serias, y si van a ocurrir, podemos evitarlas o al menos disminuirlas?*

*Finalmente, ¿hemos instruído al paciente, a los familiares y nos hemos preparado mentalmente nosotros, para la posible presentación de esas complicaciones?*

*No debe haber duda en nuestra mente de cuáles son los factores que en gran parte determinan los efectos de la cirugía sobre el aparato respiratorio. En orden de importancia son:*

### **1. Enfermedad Pulmonar Pre-existente:**

*Bajo este término englobamos todos aquellos pacientes, que tienen algún trastorno obstructivo de las vías respiratorias. No solo el enfisematoso crónico o el bronquítico que todo el mundo diagnostica fácilmente si no que tenemos que tener claro qué personas que se consideran "saludables" si son fumadoras, por serlo tienen cierre prematuro de las vías respiratorias pequeñas, lo cual constituye el principal factor fisiopatológico de las complicaciones respiratorias post-operatorias.*

*Este grupo así constituído tiene más del 70 por ciento de atelectasias y broncopulmonías post-operatorias, si se comparan con una incidencia de solo el 3 por ciento en las personas que tienen funciones pulmonares normales antes de la cirugía. Esta cifra de por sí es razón suficiente para que tengamos la curiosidad de identificar a esos pacientes antes de operarlos.*

### **2. Sitio de la incisión:**

*La cirugía abdominal alta, conlleva mayor peligro de complicaciones que la torácica aun en pacientes "normales". Esto es así por ser los músculos abdominales músculos expiratorios y por el impedimento que la incisión ejerce sobre el mecanismo de la tos que induce a la retención de secre-*

ciones intrabronquiales y puede ser la causa principal de atelectasias y pulmonías post-operatorias.

Los procedimientos quirúrgicos torácicos no están libres de complicaciones y en los pacientes con enfermedad pulmonar previa la frecuencia de complicaciones (desde leves a severas) sube a más del 75 por ciento.

### 3. Medicación analgésica y narcótica:

Este tipo de medicación tan ampliamente usado se ha demostrado que ejerce un efecto nocivo al aparato respiratorio. Los mecanismos son varios pero debe alertarnos para usarlos con la mayor precaución y tacto.

### 4. Hábito de fumar:

El solo hecho de que el paciente fume más de 20 cigarrillos al día multiplica por cuatro la frecuencia de complicaciones pulmonares. El dejar de fumar por dos o tres días pre-operatoriamente, no se ha demostrado que sea tan efectivo como se ha pensado hasta el presente.

### 5. Edad:

La mortalidad post-operatoria es 16 veces mayor, y la morbilidad es 21 veces mayor en pacientes mayores de 60 años si se comparan con grupos entre 16 y 39 años. Si pensamos que la mayor parte de los pacientes de cirugía electiva pasan de 60 años, nos veremos forzados a concluir que es en estos casos por sufrir la frecuencia mayor de complicaciones los más necesitados de una evaluación pre-operatoria para evitarnos sorpresas desagradables y estadías prolongadas.

### 6. Obesidad:

Esto es un factor de riesgo que multiplica por dos la frecuencia de complicaciones. No solo para el paciente con una obesidad exagerada, si no también, con obesidad moderada del 30 al 40 por ciento sobre el peso ideal.

En un estudio reciente hecho para el gobierno de Francia, se pudo demostrar que si se identifica a los pacientes con trastornos respiratorios antes de la cirugía y se empieza un programa de tratamiento pre, peri, y post-operatorio se acortaba en un 40 por ciento la estadía en el hospital y se disminuiría en más de un 50 por ciento la frecuencia de las complicaciones post-operatorias. Esto significaba para el gobierno francés más de 800 millones de dólares al año. Estos hallazgos son aplicables a cualquier país del mundo. Si sumamos a este factor económico el precio inmenso en sufrimientos, ansiedades, pérdida de horas de trabajo y en última instancia en pérdida de vidas que pudieron salvarse, estamos obligados a someter a nuestros pacientes quirúrgicos a un ligero escrutinio de su función respiratoria para hacer del día de la "operación" UN RIESGO CALCULADO.

Ramón E.. Figueroa Lebrón, MD  
Presidente Sección Neumología

## Programa Científico

MIÉRCOLES, NOVIEMBRE 7, 1979

### Sesión Científica A \*

Salón Núm. 3

9:00 - 12:00 - COURSE ON LUNG DISEASES

Ramón Figueroa-Lebrón, MD, Moderador

- 9:00-9:40 The Preparation of the Patient for Surgery  
T. J. DeKornfeld, MD
- 9:40-10:00 Defense Mechanisms of the Lung  
R. Figueroa, MD
- 10:00-10:15 Coffee Break
- 10:15-10:55 Asbestosis  
H. Kazemi, MD
- 10:55-11:15 The Newer Pulmonary Function Test  
A. Córdova, MD
- 11:15-11:55 Rehabilitation of the Patient with Severe Obstructive Airway Disease  
T. J. DeKornfeld, MD

12:00 - 1:00

Salón Núm. 3

### CONFERENCIA MAGISTRAL

EUGENIO FERNANDEZ GARCIA\*\*

Modern Aspects in the Treatment of Bronchial Asthma

H. Kazemi, MD

Chief Pulmonary Disease Section

Massachusetts General Hospital

### MIÉRCOLES

### SESIONES DE LA MAÑANA

### Sesión Científica B \*

Salón Núm. 4

9:00-12:00 - CURSO ENFERMEDADES DEL COLÁGENO - ASPECTOS TERAPEUTICOS  
Esther González-Parés, MD - Moderador

- 9:00-9:30 Artritis Reumatoide  
R. González, MD
- 9:30-10:00 Lupus Eritematoso Sistémico  
E. González, MD
- 10:00-10:15 Receso
- 10:15-10:45 Artritis Monoarticular Infecciosa  
C. Fernández, MD
- 10:45-11:15 Artritis Gotosa  
S. de la Cruz, MD
- 11:15-11:55 Panel - Preguntas y Respuestas

### Sesión Científica C \*

Salón Núm. 2

9:00-12:00 PURDUE FREDERICK RESEARCH  
AWARD COMPETITION  
José M. Torres-Gómez, MD - Moderador

- 9:00-9:13 Mechanisms of Reentrant Supraventricular Arrhythmias During Programmed Electrical Stimulation  
Migdalia González, MD  
Juan M. Aranda, MD  
Esteban Linares, MD  
Edgardo Hernández, MD  
Guillermo Cintrón, MD
- 9:13-9:26 Does the Liver Modify Antigenicity?  
Manuel Castillo, MD  
Eduardo A. Santiago Delpín, MD  
Esteban Moreno, MD
- 9:26-9:39 Increased Pharyngeal Bacterial Colonization During Viral Illness  
Z. Fuxench, MD  
M. Nevárez, BSMT  
C. H. Ramírez-Ronda, MD

\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (3 créditos)

\*\*Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (1 crédito)

\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (3 créditos)



MIÉRCOLES

SESIONES DE LA MAÑANA

- 9:39-9:52      Intraabdominal Providone Iodine Lavage in Experimental Peritonitis  
                  José R. Ortiz-Feliciano, MD  
                  Manuel E. Lores, MD  
                  Pedro J. Rosselló, MD
- 9:52-10:05      Penicillin Susceptibility Patterns of Gingival Organisms of Rheumatic Fever Patients on Prophylaxis  
                  B. Christenson, MSIV  
                  D. Vera, BSMT  
                  H. Delgado, MD  
                  A. Martínez-Picó, MD  
                  C. H. Ramírez-Ronda, MD
- 10:05-10:18      Carcinoma of the Stomach: Experience at the University District Hospital  
                  Manuel E. Lores, MD  
                  Pedro J. Rosselló, MD
- 10:30-10:43      Comparative Clinical Effectiveness of Cefamandole and Cefazolin in Uncomplicated Urinary Tract Infections: A Prospective Randomized Trial  
                  A. Lugo, MD  
                  D. Vera, BSMT  
                  R. H. Bermúdez, MD  
                  C. H. Ramírez Ronda, MD
- 10:43 - 10:56      The Spectrum of Left Ventricular Wall Motion During the Isovolumic Relaxation Period  
                  José Martínez, MD  
                  Pablo I. Altieri, MD  
                  Mary Torres, BS  
                  Ernesto E. Guerra, MS  
                  Lirio del Valle, BS
- 10:56 - 11:09      Toxoplasmosis Serologic Survey of 100 Subjects in Puerto Rico: A Pilot Study  
                  H. Gorbea, MD  
                  M. Medina, MS  
                  C. H. Ramírez Ronda, MD

MIÉRCOLES

SESIONES DE LA MAÑANA

- 11:09-11:22      Proctosigmoidoscopia como Método de Diagnóstico: Revisión de 2,789 Sigmoidoscopías Hospital de Veteranos  
                  Marcelo Obén, MD  
                  Pedro Rosselló, MD  
                  Reynold López, MD
- 11:22-11:35      Role of Teichoic Acids on the Adherence of *Staphylococcus aureus* to Damaged Canine Aortic Valves In Vitro  
                  J. Morales, MD  
                  A. Tomasini, MD  
                  C. H. Ramírez Ronda, MD
- 11:35-11:48      Response to Parathyroid Hormone in Patients with Recurrent Nephrolithiasis  
                  S. Amill, MD  
                  L. Lespier Dexter, MD  
                  C. Rivera, MS

Sesión Científica D \*

Salón Número 1

9:00-12:00 - TRASPLANTES DE RIÑÓN EN PUERTO RICO

E. A. Santiago Delpín, MD - Moderador

- 9:00-9:12      El Problema de la Enfermedad Renal en Puerto Rico y su Tratamiento con Diálisis y Trasplante  
                  Rafael Ramírez-González, MD
- 9:15-9:27      Técnicas y Complicaciones Urológicas en Trasplante Renal  
                  Andrés Acosta-Otero, MD  
                  Roberto Fortuño, MD
- 9:30-9:42      El Donante de Riñón: Resultados en Puerto Rico  
                  Ernesto Rivé-Mora, MD  
                  José H. Amadeo, MD

\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)

\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)

## MIÉRCOLES

## SESIONES DE LA MAÑANA

9:45-9:57	Composición Genética del Puertorriqueño Desde el Punto de Vista de Histocompatibilidad Edna Nettleship, MS
10:00-10:12	¿Aumenta la Isquemia la Antigénicidad de un Órgano? Magda Sofía Rodríguez, MS IV E. A. Santiago-Delpín MD
10:15-10:30	Receso (15 minutos)
Rafael Ramírez González, MD - Moderador	
10:30-10:42	Resultados del Programa de Trasplante Renal de Puerto Rico E. A. Santiago Delpín, MD
10:45-11:12	Radionúclidos: Técnica Indispensable en el Seguimiento del Paciente Trasplantado Julio Víctor Riviera, MD
11:15-11:27	Metabolismo de Calcio Después del Trasplante Laura Lespier, MD
11:30-11:42	Función Sexual Después del Trasplante Renal Albert Vázquez, MD
11:45-11:57	¿Se Rehabilita el Paciente Trasplantado? David Matos Alvarado, MS

12:00-1:00

Salón Número 3

CONFERENCIA MAGISTRAL  
EUGENIO FERNANDEZ GARCIA\*\*

1:00 - 2:00 - ALMUERZO

## MIÉRCOLES

## SESIONES DE LA TARDE

## Sesión Científica E \*

Salón Núm.4

2:00 - 5:00	COURSE ON PHYSICAL MEDICINE AND REHABILITATION Rafael Berrios Martínez MD - Moderador
2:00-2:25	EMG and Conduction Velocities in Hansen's Disease Luis F. García, MD
2:25-2:50	The Blink Reflex Sergio López, MD
2:50-3:15	Carpal Tunnel Syndrome Iván G. Martínez, MD
3:15-3:40	Cardiac Rehabilitation Florencio Sáez, MD
3:40-3:55	Break
3:55-5:00	Panel: Painful Non-Articular Musculoskeletal Conditions Herman J. Flax, MD Benigno Fernández, MD Moisés Santiago, MD Arturo Arché, MD

## Sesión Científica F \*

Salón Núm. 2

## 2:00-5:00 - COURSE ON PSYCHIATRY

William Galíndez Antelo, MD - Moderator

2:00-2:45	Differential Diagnosis of the Acute Psychosis: Organic and Non-Organic, Management and Treatment William Anderson, MD
2:45-3:30	Test Tube Babies: Ethical Medical and Psychological Issues Bertram Brown, MD
3:30-3:45	Break
3:45-4:30	Tardive Dyskinesia Jorge Pérez-Cruet, MD
4:30-5:00	Questions and Answers

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\*\*Acreditación para el Programa de Educación Médica Continuada en Categoría I (1 crédito)

\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)

**MIÉRCOLES**

**SESIONES DE LA TARDE**

**Sesión Científica G\***

**Salón Número 1**

**2:00-5:00 - PSRO Y PUERTO RICO**

**Rosa E. Fiol, MD - Moderador**

- |           |                                      |
|-----------|--------------------------------------|
| 2:00-2:35 | Introducción                         |
|           | R. Fiol, MD                          |
| 2:35-3:10 | Objetivos 1978-79                    |
|           | K. Ramírez, MD                       |
| 3:10-3:30 | Preguntas y Respuestas               |
| 3:30-3:45 | Receso                               |
| 3:45-4:15 | Análisis de Perfiles de Médicos      |
|           | K. Ramírez, MD                       |
| 4:15-4:45 | Análisis de Perfiles Institucionales |
|           | R. Fiol, MD                          |
| 4:45-5:00 | Preguntas y Respuestas               |

**Sesión Científica H \***

**Salón Número 3**

**2:00-5:00 - AMBULATORY MEDICINE - COURSE  
 I - "METABOLISM"**

**Francisco Aguiló, MD, Moderator**

- |             |   |
|-------------|---|
| 2:00 - 2:30 | Pathophysiology of Hyperlipemia                       |
| 2:30 - 3:00 | Clinical and Laboratory Evaluation<br>of Hyperlipemia |
| 3:00 - 3:30 | Management of Hyperlipemic Patients                   |
| 3:30 - 3:45 | Break   |
| 3:45 - 4:15 | Hyperurecemia   |
| 4:15 - 5:00 | Questions and Answers                                 |

**MIÉRCOLES, NOVIEMBRE 7, 1979**

**7:30 – 9:00 P. M.**

**PANEL: "LENGUA Y MEDICINA"**

**Auspiciado por**

**Asociación Médica de Puerto Rico  
 Fundación Puertorriqueña de las Humanidades  
 Ateneo Puertorriqueño**

**Maestro de Ceremonias: Carlos H. Ramírez Ronda, MD  
 Moderador: José M. Torres Gómez, MD**

***Panelistas:***

**José Ramírez Rivera, MD  
 Rodrigo Menéndez Corrada, MD  
 José Taveras, MD**

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## JUEVES, NOVIEMBRE 8, 1979

## SESIONES DE LA MAÑANA

## Sesión Científica I \*

## Salón Número 3

9:00-12:00 - COURSE ON GASTROENTEROLOGY

Juan R. Colón Pagán, MD - Moderator

- 9:00-9:15 Biliary Fistula: Case Presentation  
Jorge Mayoral, MD
- 9:15-9:30 Surgical Management of Hepatic Cysts  
Enrique Vázquez-Quintana, MD
- 9:30-9:45 Adjuvant Radiotherapy in Carcinoma of Rectum  
José Tomé, MD
- 9:45-10:00 Diagnostic and Therapeutic Colonoscopy  
Filiberto Colón-Rodríguez, MD
- 10:00-10:15 Interventional Radiology  
Manuel Pérez, MD
- 10:15-10:30 Break
- 10:30-10:45 Diagnostic ERCP  
Jorge Hernández Denton, MD
- 10:45-11:45 Diagnosis and Management of Reflux Esophagitis  
Robert Fisher, MD

12:00-1:00

## Salón Número 3

## CONFERENCIA MAGISTRAL "SIFRE MEMORIAL LECTURE" \*\*

"Protein Caloric Malnutrition and the GI Tract"

Fernando E. Viteri, MD

## JUEVES

## SESIONES DE LA MAÑANA

## Sesión Científica J \*

## Salón Número 4

9:00-12:00 - CURSO - MEDICINA INDUSTRIAL

Luis J.. Flores-Vilar, MD - Moderador

- 9:00-9:45 Urología en la Medicina Industrial  
Hernán Carrión, MD
- 9:45-10:30 Aplicaciones Quirúrgicas Cardiovasculares en la Medicina Industrial  
Agustín Arbulú, MD
- 10:30-10:45 Receso
- 10:45-11:30 El Potencial Evocado Cerebral en la Clínica Médica y en la Industrial  
Juan Rodríguez, MD
- 11:30-11:55 Preguntas y Respuestas

## Sesión Científica K \*\*

## Salón Número 1

9:00-11:00 - RESEARCH IN SURGERY

Pedro J. Rosselló, MD, Moderator

- 9:00-9:15 Esophageal Atresia and Tracheoesophageal Fistula  
Pedro J. Rosselló, MD  
Manuel E. Lores, MD
- 9:15-9:30 Soft Tissue Sarcoma in Children  
Manuel H. Castillo, MD  
Pedro J. Rosselló, MD  
Roberto Novoa, MD
- 9:30-9:45 Tres Casos de Origen Anómalo de la Arteria Coronaria Izquierda desde la Pulmonar Principal  
José Ramón Gómez, MD  
Jorge Valdés, MD  
Héctor Rodríguez, MD

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\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)

\*\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (2 créditos)

JUEVES		JUEVES	
SESIONES DE LA MAÑANA		SESIONES DE LA MAÑANA	
9:45-10:00	Multiple Pregnancy: The Second Twin. Emilio J. Gómez, MD Nilda M. Vázquez, MD	Sesión Científica L *	Salón Número 2
10:00-10:15	A Puerto Rican Female with Homocystinuria - Case Presentation María A. Toro-Solá, MD A. I. Muñoz, MD	9:00-12:00 – THE MULTIDISCIPLINARY APPROACH TO LEARNING DISABILITIES	
10:15-10:30	Cryptorchidism, Review of 430 Cases. Roberto Novoa, MD Pedro J. Rosselló, MD	Luis P. Sánchez Longo, MD - Moderator	
10:45-11:00	Anovulatory Infertility Associated with Cervix Incompetence Walter M. Pinedo, MD. Rafael Rodríguez Acevedo, MD	9:00-9:10 Welcome Remarks Norman Maldonado, MD	
		9:10-10:10 Special Learning Disabilities Julio Bernardo de Quirós, MD	
		10:10-10:30 Questions and Answers	
		10:30-10:45 Recess	
		10:45-11:45 Educational Treatment and Prognosis on Learning Disabled Child Margaret Jo Sheperd, MD	
		11:45-12:00 . Questions and Answers	
<hr/>		<hr/>	
11:00-12:00	Salón Núm. 1	12:00 - 1:00 - CONFERENCIA MAGISTRAL "SIFRE MEMORIAL LECTURE"	
PLENARY CONFERENCE***		1:00-2:00 – ALMUERZO (Cortesía de Pfizer Corporation)	
"The Pathology of the Transplanted Kidney"		<hr/>	
Introduction		SESIONES DE LA TARDE	
Jesús Vázquez, MD Soc. Médicos Graduados Universidades Españolas		Sesión Científica M *	Salón Número 2
Horacio Oliva, MD Catedrático de Patología Universidad Autónoma de Madrid		2:00-5:00 - COURSE ON ONCOLOGY Sociedad Médicos Graduados Universidades Dominicanas	
<hr/>		Rafael Sorrentino, MD - Moderator	
**Acreditación para el Programa de Educación Médica Continuada en Categoría I (2 créditos)		2:00-2:30 Chemical Carcinogenesis and the Primary Physician Angel A. Román-Franco, MD	
***Acreditación para el Programa de Educación Médica Continuada en Categoría I (1 crédito)		* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)	

## JUEVES

## SESIONES DE LA TARDE

- 2:30-3:00 Role of Nutrition in Cancer - Cause, Prevention and Treatment  
Alan Preston, PhD
- 3:00-3:30 Computerized Tomography, Ultrasound and X-Ray - An Integrated Approach  
José T. Medina, MD
- 3:30-3:45 Recess
- 3:45-4:10 Use of Estrogen Receptor in the Evaluation and Management of Breast Cancer Patient  
Reynold E. López, MD
- 4:10-4:35 Vomiting as a Precursor Sign of the Acute Abdomen in the Newborn  
Enrique Márquez, MD
- 4:35-5:00 Diagnosis and Management of Cervical Lymphadenopathy  
Rafael Sorrentino, MD

## Sesión Científica N \*

## Salón Número 4

## 2:00-5:00 - CURSO PEDIATRIA: EL NIÑO CON RETRASO EN EL CRECIMIENTO

Aurea I. Muñoz, MD - Moderador

- 2:00-2:30 Retraso Intrauterino  
Hilda Rivera de Quiñones, MD
- 2:30-3:00 Aspectos Endocrinos del Retraso en el Crecimiento  
Ana A. Rodríguez, MD
- 3:00-3:15 Receso
- 3:15-3:45 Aspectos Genéticos y Metabólicos  
María Toro-Solá, MD
- 3:45-4:15 Factores Nutricionales y Sistémicos  
Aurea I. Muñoz, MD
- 4:15-5:00 Recapitulación  
Preguntas y Respuestas

\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (3 créditos)

## JUEVES

## SESIONES DE LA TARDE

## Sesión Científica O \*

## Salón Número 1

## 2:00-5:00 - COURSE: RESEARCH IN INTERNAL MEDICINE AND PSYCHIATRY

Raúl Costas, MD, Moderator

## 2:00-2:15 Correlation of Early Post Infarction Hemodynamics and Treadmill Exercise Testing

Guillermo Cintrón, MD  
Esteban Linares, MD  
Brunilda Peña, RN  
Marta Medina, RN  
Edgardo Hernández, MD  
Migdalia González, MD  
Juan M. Aranda, MD

## 2:15-2:30 Coronary Heart Disease Risk Factors in Men with Light and Dark Skin

Raúl Costas, Jr., MD  
Mario R. García-Palmieri, MD  
Paul Sorlie, MS  
Ellen Hertzmark, MA

## 2:30-2:45 The Left Ventricular Dysfunction of Patients with Idiopathic Prolapse of the Mitral Valve

Pablo I. Altieri, MD  
Lirio Del Valle, BS  
Mary Torres, BS  
Ernesto Guerra, BS

## 2:45-3:00 Exercise Treadmill Testing in the Early and Convalescent Period After Acute Myocardial Infarction

Esteban Linares, MD  
Guillermo Cintrón, MD  
Julio E. Pérez, MD  
Edgardo Hernández, MD  
Migdalia González, MD  
Juan M. Aranda, MD

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Continuada en Categoría I (3 créditos)



JUEVES	SESIONES DE LA TARDE	JUEVES	SESIONES DE LA TARDE
3:00-3:15	Expected Risk of Coronary Heart Disease in Puerto Rican Men Raúl Costas, Jr., MD Mario R. García-Palmieri, MD Mercedes Cruz-Vidal, MD Paul Sorlie, MS	3:45	Recess
3:15-3:30	Receso	4:00	Overview of the Research in Progress in M.S. Milton Alter, MD Robert J. Slater, MD
3:30-3:45	Insulinoma G. Martínez-Rovira, MD José Amadeo, MD	4:55	Closing Remarks Ana G. Méndez
3:45-4:00	Central Nervous System Manifestation in Systemic Lupus Erythematosus Esther N. González-Parés, MD Ramón L. Ortega, MD Ivelisse Lebrón, MD	Sesión Científica Q *                      Salón Número 3	
4:00-4:15	Manejando al Deprimido Víctor Bernal y del Río, MD Eduardo Castro, MD	2:00 - 5:00 - AMBULATORY MEDICINE - COURSE II - "NUTRITION"	
4:15-4:30	A Retrospective Study of Emotional Symptoms in a Group of Women Subjected to Hysterectomy in Puerto Rico Daisy Jesurum, MD Minerva Villafañe, MD Jorge Pérez Criet, MD	Juan T. Tomasini, MD - Moderator	
4:30-4:45	Witchcraft and Psychiatry E. P. O'Malley, MC, USNR Joyce S. Strauss, MBA R. Makin, MC, USNR	2:00 - 2:30	Nutritional Profile of the P. R. Population Nelson Fernández, MD
Sesión Científica P *                      Salón Número 5		2:30 - 3:00	Drug Induced Malnutrition José J. Corcino, MD
2:00-5:00 - COURSE - MULTIPLE SCLEROSIS		3:00 - 3:30	Vitamin Therapy L. Lezzotte, MD
Luis P. Sánchez Longo, MD, Moderator		3:30 - 3:45	Recess
2:00	Welcome Pedro J. Santiago-Borrero, MD	3:45 - 4:15	Clinical Management of Obesity Nelson Fernández, MD
2:10	Epidemiology of Multiple Sclerosis Milton Alter, MD	4:15 - 5:00	Questions and Answers Panel
3:00	Organization of Regional Services for the M.S. Patients Robert Slater, MD	* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)	

\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)

## VIERNES, NOVIEMBRE 9, 1979

## SESIONES DE LA MAÑANA

## Sesión Científica R \*

Salón Número 3

9:00-12:00 - CURSO: ENFERMEDADES INFECCIOSAS

Ramón H. Bermúdez, MD, Moderador

9:00-9:30	Vacunación: Conceptos Básicos y Complicaciones C. H. Ramírez-Ronda, MD
9:30-10:00	DPT, Polio, Influenza R. H. Bermúdez, MD
10:00-10:15	Pneumovax, Meningococcia J. Morales, MD
10:15-10:30	Receso
10:30-10:45	Tifoidea y Cólera R. Quiñones, MD
10:45-11:15	Viajes al Extranjero y Vacunación G. Vázquez, MD
11:15-12:00	Preguntas y Respuestas

12:00 - 1:00

Salón Número 3

## PLENARY CONFERENCE ON INFECTIOUS DISEASES\*\*

"Cryptococcosis"

Richard J. Duma, MD  
Professor of Medicine  
Medical College of Virginia

## VIERNES

## SESIONES DE LA MAÑANA

## Sesión Científica S \*

Salón Número 4

9:00-12:00- CURSO DE CIRUGIA - EL MEDICO PRIMARIO Y LAS CIENCIAS QUIRURGICAS

Gumersindo Blanco, MD - Moderador

9:00-9:30	La Gama de la Cirugía Ambulatoria: Conceptos Generales Gumersindo Blanco, MD
9:30-10:00	Procedimientos Comunes de la Cirugía Ambulatoria Primaria Zulma González, MD
10:00-10:15	Receso
10:15-10:40	Cirugía de la Mano: Trauma e Infecciones José F. Bernal, MD
10:40-11:05	Urología Ambulatoria por el Médico Primario Roberto Fortuño, MD
11:05-11:30	Ortopedia y Manejo de Fracturas por el Médico Primario Rafael Fernández Feliberti, MD
11:30-12:00	Trauma Craniocerebral y Lesiones Intracranianas Humberto Ortiz Suárez, MD

## Sesión Científica T \*

Salón Número 1

9:00-12:00 - RESEARCH IN HEMATOLOGY AND ONCOLOGY

E. Vélez-García, MD - Moderator

9:00-9:15	Revision of the Histologic Classification in Hodgkin's Disease L. Núñez, MD J. Velázquez, MD R. Dorfman, MD E. Vélez-García, MD E. Delgado, RN
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\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)

\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)

\*\*Acreditación para el Programa de Educación Médica Continuada en Categoría I (1 crédito)

VIERNES

SESIONES DE LA MAÑANA

- 9:15-9:30 Evaluation of an Adjuvant Chemotherapy Program with Cis-Dichlorodiammine Platinum and Blcomycin Combined with Radiotherapy Prior to Surgery in Advanced Head and Neck Cancer  
C. Chicsa, MD  
N. Figuroa, MD  
E. Vélez-García, MD  
V. Marcial, MD  
J. Cintrón, MD  
J. Corcino, MD  
M. Maldonado, MD
- 9:30-9:45 Radiation Induced Liver Damage in the Dog  
J. A. Moscol, MD  
V. A. Marcial, MD  
E. Santiago Delpín, MD  
A. E. Lanaro, MD  
J. Velázquez, MD  
C. Gómez, MD
- 9:45-10:00 Acute Promyelocytic Leukemia - Histochemical Characterization, Clinical Presentation and Evaluation of 30 Patients  
J. Figuroa-Casas, MD  
J. Fradera, BS MT  
E. Vélez-García, MD  
J. Corcino, MD
- 10:00-10:15 The Role of Radiation Therapy in the Management of Carcinoma of the Endometrium  
J. Ubiñas, MD  
J. M. Tomé, MD  
V. A. Marcial, MD
- 10:15-10:30 Recess

VIERNES

SESIONES DE LA MAÑANA

- 10:30-10:45 A Randomized Trial of Methotrexate with or without Citrovorum Factor in Squamous Cell Carcinoma of the Head and Neck and Adenocarcinoma of the Breast and Colon  
E. Vélez-García, MD  
W. R. Vogler, MD  
J. Jacobs, MD  
S. Moffit, MD
- 10:45-11:00 Peyronics Disease  
J. M. Tomé, MD  
V. A. Marcial, MD  
J. Ubiñas, MD  
J. L. Ferrer, MD  
L. Nieves Valle, MD
- 11:00-11:15 Usefulness of Cytochemical Studies in the Classification of the Acute Leukemia  
Jean Fradera, BSMT  
Enrique Vélez-García, MD  
José J. Corcino, MD  
Ileana López, BSMT
- 11:15-11:30 Radiation Therapy for Carcinoma of the Prostate Limited to the Pelvis  
V. A. Marcial, MD  
J. M. Tomé, MD  
J. Ubiñas, MD
- 11:30-11:45 Misonidazole as a Sensitizer of Radiation in Head and Neck and Esophageal Carcinoma  
A. Ydrach, MD  
V. A. Marcial, MD

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\* Acreditación para el Programa de Educación Médica Continuada en Categoría I (3 créditos)



## VIERNES

## SESIONES DE LA MAÑANA

Sesión Científica U \*                      Salón Número 2

9:00-12:00 - COURSE IN OBSTETRICS AND  
GYNECOLOGY - I

A. Comas, MD - Moderator

9:00 - 10:00      Herpes Virus and other Venereally  
Transmitted Infections  
Ralph M. Richart, MD

10:00 - 10:15      Coffee Break

10:15 - 11:00      Pros and Cons of Colposcopy and  
who should use it  
Ralph M. Richart, MD11:00 - 12:00      Diagnostic Ultrasonnd in OB/GYN  
A. L. Rodríguez Rosado, MD-----  
12:00-1:00 - CONFERENCIA PLENARIA1:00-2:00 – ALMUERZO  
(Cortesía de la Cruz Azul de Puerto Rico)  
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## SESIONES DE LA TARDE

Sesión Científica V \*                      Salón Número 2

2:00- 5:00 - COURSE IN OBSTETRICS AND  
GYNECOLOGY - II

A. Comas, MD, Moderator

2:00 - 3:00          Understanding Abnormal Uterine Ble-  
eding: Etiologies and Management  
Ralph M. Richart, MD\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (3 créditos)

## VIERNES

## SESIONES DE LA TARDE

3:00 - 3:45          The Management of Vaginitis in  
Children  
Natalio Bayonet, MD

3:45 - 4:00          Coffee Break

4:00 - 5:00          Advances in the Management of Pre-  
cancerous Lesions on an Office Basis  
Ralph M. Richart, MD

Sesión Científica W \*                      Salón Número 4

2:00-5:00 - CURSO PEDIATRIA - PEDIATRIA AM-  
BULATORIA

Edna Zayas, MD, Moderadora

2:00-2:30          Tratamiento de Asma  
José E. Sifontes, MD2:30-3:00          Tratamiento de Diarrea  
Edna Zayas, MD3:00-3:30          Niños Maltratados  
O. Rodríguez, MD

3:30-3:45          Receso

3:45-4:15          Otitis y Faringitis  
A. I. León, MD

4:15-5:00          Preguntas y Respuestas

Sesión Científica X \*                      Salón Número 1

2:00-5:00 - PLASTIC SURGERY - CONCEPTS AND  
APPLICATIONS

José I. Iglesias, MD - Moderator

2:00-2:30          Breast Reduction: Indications, Uses  
and New Concepts  
Walter Benavent, MD\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (3 créditos)

VIERNES		SESIONES DE LA TARDE		SABADO, NOVIEMBRE 10, 1979	
2:30-3:00	Plastic Surgery of the Hand Miguel Vargas, MD			Sesión Científica Z *	Salón Número 3
3:00-3:15	Coffee Break			9:00-12:00 - CURSO MEDICINA AMBULATORIA IV - CARDIOLOGIA	
3:15-3:45	Rhinoplasty in Puerto Rico Alberto Sánchez, MD			Juan M. Aranda, MD, Moderador	
3:45-4:15	Gynecomastia: What to do from Cosmetic Angles? José L. Iglesias, MD			9:00-9:30	Tratamiento Médico Ambulatorio de Hipertensión Arterial Rafael Ramírez González, MD
4:15-5:00	Questions and Answers			9:30-10:00	Tratamiento Médico Ambulatorio del Paciente con Angina de Pecho Juan M. Aranda, MD
Sesión Científica Y *	Salón Número 3			10:00-10:30	Tratamiento Médico Ambulatorio del Paciente con Arritmias Cardíacas Carlos Girod, MD
2:00-5:00 - CURSO MEDICINA AMBULATORIA III REUMATOLOGIA				10:30-10:45	Receso
Alejandro Franco, MD, Moderador				10:45-11:15	Tratamiento Médico Ambulatorio del Paciente con Fallo Congestivo Car- diaco Héctor Delgado, MD
2:00 - 2:30	Estudios de Laboratorio y su Inter- pretación en el Paciente con Síntomas Reumáticos Alejandro E. Franco, MD			11:15-12:00	Panel: Preguntas y Respuestas
2:30 - 3:00	Nuevos Agentes Anti-Inflamatorios; Farmacología e Indicaciones Nydia Brugneras, MD			12:00-1:00	Salón Núm. 3
3:00 - 3:30	Evaluación del Hombro Doloroso Carlos Grovas, MD			CONFERENCIA MAGISTRAL "RAMON M. SUAREZ"***	
3:30 - 4:15	Síndromes Reumáticos Frecuentes en la Práctica General Radamés Sierra, MD			"Cardiología — Presente, Pasado y Futuro" Introducción: Norman Maldonado, MD Rector, Ciencias Médicas, UPR Efraín García, MD Catedrático Asociado Medicina Baylor College of Medicine	
4:15 - 5:00	Panel: Preguntas y Respuestas			1:30	Salón El Teatro
				ALMUERZO — TOMA DE POSESION del nuevo Presidente de la Asociación Médica Dr. Gerardo Sanz Ortega	

\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (3 créditos)

\* Acreditación para el Programa de Educación Médica Con-  
tinuada en Categoría I (3 créditos)

\*\*Acreditación para el Programa de Educación Médica Con-  
tinuada en Categoría I (1 crédito)

SABADO

NOVIEMBRE 10, 1979

## Sesión Científica AA \*

Salón Número 2

9:00 - 11:00 - AMBULATORY MEDICINE - COURSE  
V - "ENDOCRINOLOGY"

José Hernán Martínez, MD - Moderator

9:00-9:30      Diabetes Mellitus

9:30-10:00      Understanding Thyroid Tests

10:00- 10:15      Break

10:15-10:45      Evaluation and Management of  
Thyromegaly

10:45-11:00      Questions and Answers

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11:00- 12:00 - CONFERENCIA ESPECIAL ENDO-  
CRINOLOGIA \*\*"Seudo Hermafroditismo Masculino: Clasificación y  
Diagnóstico Diferencial"Mario Foz Salas, MD  
Catedrático Asociado  
Universidad Autónoma de Barcelona  
-----\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (2 créditos)\*\*Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (1 crédito)

SABADO

NOVIEMBRE 10, 1979

## Sesión Científica BB \*

Salón Número 4

9:00-12:00 - RESEARCH IN INFECTIOUS DISEASES  
AND TROPICAL MEDICINE

C. León-Valiente, MD, Moderator

9:00-9:15      Amikacin Sulfate Levels in Human  
Bile

R. H. Bermúdez, MD

A. Lugo, MD

J. Morales, MD

J. H. Amadeo, MD

C. H. Ramírez Ronda, MD

9:15-9:30      Comparative In Vitro Activity of Oral  
Cephalosporins

P. Harrington, MD

M. Nevárez, BSMT

Z. Echevarría, BSMT

R. H. Bermúdez, MD

C. H. Ramírez-Ronda, MD

9:30-9:45      Experiences with Malignant External  
Otitis - A New Complication of Dia-  
betes Mellitus

Velia Toledo, MD

Enrique Vicens, MD

Ismael Rodríguez, MD

9:45-10:00      Gentamicin Resistance of Gram-Nega-  
tive Bacilli - A Study of 498 Strains

J. Morales, MD

R. H. Bermúdez, MD

C. H. Ramírez Ronda, MD

10:00-10:15      Human Schistosomiasis Mansonii in  
Puerto Rico: A Limited Prevalence  
Survey.

G. V. Hillyer, PhD

R. Lluberes, BSMT

C. H. Ramírez Ronda, MD

10:15-10:30      Coffee Break

\* Acreditación para el Programa de Educación Médica  
Continuada en Categoría I (3 créditos)



SABADO

NOVIEMBRE 10, 1979

- 10:30-10:45      Toxoplasma Antibodies in Chronic Renal Patients  
                         S. Aldarondo, MD  
                         H. Gorbea, MD  
                         M. Medina, MS  
                         R. Ramírez, MD  
                         C. H. Ramírez Ronda, MD
- 10:45-11:00      In Vitro Activity of Compound LY127935: Comparison with Cephalosporins and Aminoglycosides  
                         C. H. Ramírez Ronda, MD  
                         M. Nevárez, BSMT  
                         Z. Echevarría, BSMT  
                         R. H. Bermúdez, MD
- 11:00-11:15      Infección por Tuberculosis en los Estudiantes de Medicina  
                         José E. Sifontes, MD
- 11:15-11:30      Disk Susceptibility Patterns of Clinical Isolates at VAIL during 1978  
                         M. A. Medina, MS  
                         R. H. Bermúdez, MD  
                         C. H. Ramírez Ronda, MD
- 11:30-11:45      Cefaclor in Soft Tissue Infections  
                         A. Lugo, MD  
                         F. Regis, MD  
                         R. H. Bermúdez, MD  
                         C. H. Ramírez Ronda, MD
- 11:45-12:00      Comparative Antibacterial Activity of 14 Cephalosporins Against 400 Bacteremic Strains of Gram-Negative Bacilli  
                         J. Gutiérrez, MD  
                         M. Nevárez, MD  
                         Z. Echevarría, BSMT  
                         R. H. Bermúdez, MD  
                         C. H. Ramírez Ronda, MD

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12:00-1:00 - CONFERENCIA MAGISTRAL  
1:30 - El Teatro - ALMUERZO - TOMA DE POSESION  
Nuevo Presidente de la AMPR-Dr. Gerardo Sanz

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## BREAST PAIN: A SYMPTOM OF CERVICAL RADICULOPATHY

*La Ban, M. M., Meerschaert, J. R., et al — Arch. Phys. Med. Rehabil. 60: 315-317, 1979 . .*

Los autores presentan un estudio hecho en 18 mujeres con dolor crónico de mama. Todas tenían evaluaciones extensas de la mama, pero no diagnósticas de ninguna enfermedad, incluyendo 10 mamografías y 4 biopsias; todas las pacientes fueron tratadas con éxito usando tracción cervical.

Cada paciente tenía evidencia clínica o electromiográfica de radiculopatía cervical. Quince pacientes tenían evidencia radiológica de espondilosis cervical, principalmente en los niveles C-6 y C-7.

Según ellos, entre los síntomas mejor reconocidos de la radiculopatía cervical se encuentra la angina cervical; sin embargo, el dolor de pecho persistente como síntoma primario no se reconoce tan fácilmente. En ambos casos, la identificación del origen radicular del dolor, con sus diferentes implicaciones pronósticas y terapéuticas puede ayudar a aliviar la molestia física y psicológica del paciente.

(Sometido por Verónica Rodríguez, MD, VAH)

## OBSTACLES TO THE REHABILITATION OF DISABILITY BENEFITS RECIPIENTS

*David Schlenoff, Ed. D — J. of Rehabil. 45: 2, 56-58, 1979*

El autor del artículo se refiere al hecho de que,

aunque el Seguro de Incapacidad del Seguro Social, Compensación a los Trabajadores y la Asistencia Pública, fueron creados para ayudar en la rehabilitación de los incapacitados, en realidad lo que hacen es reducir los incentivos económicos para trabajar. El dinero para compensaciones parece estar más disponible ahora que antes, siendo obligatorio para muchos patronos el tener algún tipo de seguro para sus trabajadores.

Numerosas compañías aseguradoras privadas se han interesado en este aspecto de la rehabilitación, y algunas emplean personal médico, a la vez que "expertos vocacionales", que colaboren con sus clientes en el período de ajuste al retornar al trabajo tras estar incapacitados parcial o totalmente, debido a un accidente.

No obstante los esfuerzos del equipo de rehabilitación, muchos individuos permanecen desempleados y dependientes después que han recibido beneficios por incapacidad. Hay que prestar atención a este fenómeno, porque el número de reclamaciones a las compañías de seguros se hace cada vez mayor y el consejero de rehabilitación debe entender los factores que contribuyen a una indebida dependencia en los pagos por incapacidad para poder utilizar efectivamente el tiempo y el esfuerzo prestado en ayudar al cliente a retornar al trabajo.

Los factores principales son:

1. A veces el empleo que se ofrece no representa una ganancia sobre lo que recibe el paciente por su incapacidad.

2. La inseguridad en la permanencia del empleo ofrece poco incentivo para renunciar al pago fijo y seguro que se recibe por incapacidad.

3. Muchos incapacitados ven la oferta de empleo como una amenaza a su ingreso por incapacidad.

4. Debido a las ganancias secundarias que resulten por la incapacidad, el paciente tiende a minimizar o maximizar las limitaciones de trabajo que resultan de una condición crónica.

Los autores recomiendan estudios más extensos de las ramas psicovocacionales de las agencias de seguros en torno al problema de la incongruencia entre las metas de rehabilitación y los incentivos negativos para retornar al trabajo de los individuos recibiendo compensación por incapacidad.

(Sometido por Verónica Rodríguez, MD, VAH)

## CONGENITAL MUSCULAR DYSTROPHY

*Jones, R., Khan, R., Hughes, S., Dubowitz, V. - Journal of Bone and Joint Surgery: 61-B, 13-17, 1979.*

Los autores hacen una revisión de los casos de Distrofia Muscular Congénita referidos al Hospital Hammersmith entre 1972 y 1977. Los 21 casos recopilados tenían historias de problemas ortopédicos al nacer, varios grados de debilidad muscular o, atraso en su desarrollo motor; todos con inteligencia normal. El diagnóstico en 21 de los casos fue tardío (promedio 6.6 años de edad). Entre ellos algunos desarrollaron contracturas severas que interfieren con el caminar, otros están confinados a sillones de ruedas y tres han muerto por complicaciones médicas.

De otros siete pacientes diagnosticados tempranamente (promedio de 1.7 años de edad), y que recibieron adecuadamente tratamiento ortopédico y de fisioterapia, hay cinco que pueden caminar, algunos con ayuda mecánica, y dos en proceso de hacerlo. Los autores demuestran que sospechar y hacer el diagnóstico tempranamente puede significar gran diferencia en el pronóstico de la calidad de vida de sus pacientes.

(Sometido por Frank W. López, MD, VAH)

## PRENATAL DIAGNOSIS OF DUCHENNE'S MUSCULAR DYSTROPHY

*Maurice J. Mahoney, et al - New England J. of Medicine November 3, 1977. 297: 18 : 968-973.*

Dos embarazos de alto riesgo para Distrofia Muscular recesiva ligada al sexo (Duchenne type) fueron estudiados a 18 y 20 semanas de gestación. Sangre fetal se obtuvo por aspiración transplacentaria para determinación de C. P. K. La actividad de CPK en el primer caso fue de 96 I.U. por litro de plasma, comparado con un control de 0-150 I.U./lts. en 16 embarazos no a riesgo para Distrofia Muscular (tipo Duchenne). El embarazo fue a término y el bebé es normal.

En el segundo bebé a riesgo, el C. P. K. fue de 540 U.I./litr. La sangre fetal demostró considerable hemólisis, lo que constituye un hallazgo infrecuente. Luego de aborto terapéutico, el examen microscópico por luz, fase y microscopio electrónico demostró los hallazgos característicos de la distrofia tipo Duchenne en músculos, incluyendo variación en los diámetros de las fibras musculares y disminución en el número de fibras por fascículo. Los casos ilustran el uso potencial de aspiración de plasma fetal para el diagnóstico prenatal de la Distrofia Muscular tipo Duchenne usando el C.P.K. como guía.

(Sometido por José A. Arabia, MD, VAH)

## STROKE RECOVERY: HE CAN, BUT DOES HE?

*Andrews, K., - Rheumatol. & Rehab., 18: 1 - 43-48, 1979*

Para señalar la motivación del paciente para la recuperación después de haber sufrido un derrame cerebral, 29 pacientes consecutivos, que obtuvieron notas pasables en una prueba mental, fueron evaluados en actividades del diario vivir mientras estaban en el hospital y luego en su casa. Hubo una variación amplia entre lo que los pacientes podían hacer en el hospital y en su casa. Sobre 33 por ciento de los pacientes hicieron peor en su casa en cada una de las actividades del diario vivir. En 52 por ciento de los casos, los acom-



pañantes en los hogares aseguran que los pacientes no hicieron 2 o más actividades que eran capaces de hacer en el hospital. Este resultado estaba *más relacionado* con las actividades de los pacientes y de las personas que los atendían, que con las características del derrame en sí. La mayoría de aquellos pacientes, cuyas ejecuciones eran pobres en su casa, comenzaron la rehabilitación después de 3 meses de haber ocurrido el derrame. Los resultados enfatizan el papel del que atiende al paciente en el hogar, y sugiere la necesidad de mejorar la rehabilitación centralizada en el hogar.

### INCREASE OF MUSCLE STRENGTH FROM ISOMETRIC QUADRICEPS EXERCISES AT DIFFERENT KNEE ANGLES

Margareta Lindh. - *Scand J Rehab Med* 11:33-36, 1979.

Ejercicios isométricos para el cuádriceps se llevaron a cabo en dos ángulos diferentes para la rodilla, a 15° y 60°, respectivamente. La fuerza máxima fue medida en ambas posiciones — antes y después del entrenamiento — en 10 mujeres saludables. Ambas piernas fueron ejercitadas, una en cada posición. El propósito era desarrollar unas recomendaciones prácticas para escoger la posición más adecuada al entrenamiento. El aumento en la fuerza fue mayormente específico al ángulo en el cual la rodilla fue ejercitada. Se sugiere que el ejercicio isométrico preferiblemente se haga a diferentes ángulos en la rodilla para asegurar un aumento total en la fuerza. Los ejercicios isométricos mejoran la fuerza dinámica a baja velocidad, pero no en alta.

Sometido por Rafael Seín, MD, VAH)

### SCIATIC NERVE PALSY AS A COMPLICATION OF BLEEDING FOLLOWING HIP SURGERY

Fleming, R. E., Michelsen, D. B., Stinchfield, F. E. - *The Journal of Bone and Joint Surgery*. 61: A1:37-39, 1979.

En un grupo de 5 pacientes que desarrollaron parálisis del nervio ciático como resultado de hemorragia y hematoma después de cirugía de cadera, 4 de ellos estaban recibiendo anti-coagulantes como tratamiento profiláctico. A uno de los pacientes no se le administró tratamiento alguno, y durante el seguimiento persistió con síntomas motores y sensitivos incapacitantes. El quinto paciente murió tres semanas después del comienzo del cuadro clínico, con la neuropatía aún presente. Evidencia de hemorragia en la vecindad del nervio ciático es: dolor en región glútea y espalda baja, equimosis sobre estas áreas, inflamación del muslo, dolor a la palpación del nervio ciático y un déficit nervioso ciático en la extremidad interior ipsilateral de un paciente recientemente sometido a cirugía de cadera. El reconocimiento temprano y la decompresión quirúrgica evitan el daño nervioso irreversible.

(Sometido por Jesús A. Maldonado, VAH)

### AMINOFILINA INTRAVENOSA

*Chest* - Vol. 76 No. 1 - 7/79

Desde la introducción de los métodos de medición de la Teofilina sérica se ha inundado la literatura médica de artículos relacionados con el uso y cantidades de Aminofilina en el paciente asmático. Para resumir un poco los conocimientos adquiridos recientemente y para evitar las confusiones, el autor del artículo pone en relieve lo más significativo.

a. La vida media de la teofilina varía entre 3 y 12.8 horas con una media de 7.5 en adultos y desde 1.5 a 7.8 horas con una media de 3.4 horas en niños.

La media vida se prolonga con:

1. Fallo cardíaco congestivo
2. Disfusión hepática
3. Ingestión de Troleandomicina y Eritromicina.
4. Fiebre
5. Infecciones virales del tracto respiratorio

alto.

La media vida se acorta con:

1. Administración prolongada de Fenobarbital.
2. En Fumadores
3. Algunos factores dietéticos.

La depuración renal de teofilina puede variar en el mismo paciente de día a día.

La media vida en el infante prematuro está marcadamente alargada pero en el paciente envejeciente no varía casi nada, pero como el volumen en donde la droga se distribuye es menor es necesario usar en ellos dosis más bajas.

En pacientes con pH ácido el volumen en donde la droga se distribuye es más alto de modo que los pacientes con acidosis pueden tolerar dosis mayores de Aminofilina intravenosa.

La dosis de 5.6 mg/kg de Aminofilina seguida de 0.9 mg/kg/hora resulta en niveles de teofilina sérica más altos que los deseables.

Las incidencias de convulsiones y muertes debidas a toxicidad por teofilina se siguen reportando aún con niveles menores de 2.5 ug/ml aunque la mayor frecuencia de estas complicaciones ocurren cuando el nivel de teofilina sérica es mayor de 47 ug/ml.

Como la determinación de teofilina sérica no está disponible para todos los médicos que prescriben Aminofilina intravenosa las siguientes reglas simples se deben observar:

1. Es mejor pecar de conservador que de muy agresivo. La dosis de Aminofilina intravenosa no debe ser mayor de 1gm/día o 0.5 mg/kg/hr. a menos que los niveles de teofilina sean bien accesibles.
2. Manifestaciones de toxicidad y en especial náuseas, vómitos y dolor de cabeza ocurren a diario aún con estas dosis bien pequeñas.
3. Estas dosis se deben reducir aún más en pacientes con fallo cardíaco, enfermedades hepáticas, en los envejecientes (75) y en aquellas situaciones en que sabemos la media vida estará prolongada.
4. En niños la dosis de mantenimiento está entre 9- y 39.6 mg/kg/día. Una dosis media

de 15 mg/kg/día es la más recomendada para éstos.

5. Por último hay que recordar que el tratamiento de asma no debe descansar solo en teofilina y que la combinación con otras drogas hace posible el uso de menores cantidades de aquellas.

(Sometido por Ramón Figueroa Lebrón, MD)

## SAFETY OF CHANGING INTRAVENOUS DELIVERY SYSTEMS AT LONGER THAN 24-HOURS INTERVALS

*Annals of Internal Medicine* 1979; 91: 173-1978.

Routinely changing the intravenous fluid containers and administration set every twenty hours is widely practiced to reduce the risk of septicemia due to contamination. A prospective study has been recently done to determine if changing at longer intervals could be justified. At the conclusion of infusion therapy, both the cannula and an aliquot of remaining fluid were cultured quantitatively. A total of 790 infusions were studied and it was determined that routinely replacing the delivery system every 48 hours seems to be justified and could result in considerable savings to hospitals.

(Submitted by Ramón H. Bermúdez, MD)

## USE OF COMPUTARIZED TOMOGRAPHY IN NONSURGICAL MANAGEMENT OF BRAIN ABSCESS

*Edward B. Rotheram, Jr., MD, Laïbe A. Kessler, MD, Archives of Neurology, Vol. 36, Number 1, January 1979.*

The authors discuss two cases of multiple brain abscess treated successfully with intensive antibiotics

and followed by CAT scans. This method of management has intrinsic hazards since the infecting organism is not identified and surgical decompression by aspiration is not carried out. But the authors rightfully point out that bacterial flora of most brain abscesses is polymicrobial and predominantly anaerobic and that this has led them to use penicillin G I.V. with tetracycline or chloramphenicol for initial treatment — the penicillin for at least six weeks. In one case steroids were used. Both cases were followed with frequent CAT scans and the brain structures ultimately returned to normal. If the initial response is not favorable, then surgery can be resorted to.

(Submitted by Nathan Rifkinson, MD)

### MAXIMAL SUPINE EXERCISE HEMODYNAMICS AFTER OPEN HEART SURGERY FOR FALLOT'S TETRALOGY

*Cumming, G. C. — British Heart Journal, 41: 683-691, 1979.*

Se estudiaron los efectos hemodinámicos de ejer-

cicio máximo en 29 niños operados de Tetralogía de Fallot entre 1 y 5 años atrás. La edad en el momento de la cirugía fue entre 5 y 14 años y en el momento del estudio fue entre 6 y 16 años.

De acuerdo al status post operatorio se clasificaron en 5 grupos: Grupo 1- con gradiente pulmonar menos de 20 mm (11 ptes.); grupo 2- con gradiente pulmonar sobre 20 mm (7 ptes); grupo 3 - con defecto interventricular residual  $<1.25:1$  (4 ptes); grupo 4- con defecto interventricular y gradiente pulmonar significativo (5 ptes); grupo 5- con bloqueo completo y marcapasos, pero con buenos resultados quirúrgicos (2 ptes).

Casi todos demostraron elevación de la presión en el ventrículo derecho sin evidencia angiocardiográfica de obstrucción al tracto de salida, y 33 por ciento tuvieron una elevación en la presión diastólica-final derecha.

La capacidad al ejercicio, al igual que el índice cardíaco, volumen de eyección, y gasto cardíaco estuvieron en la parte "baja" de lo normal pero nunca menos que el valor normal.

Los pacientes en los grupos 4 y 5, con resultados quirúrgicos pobres, los valores fueron ligeramente inferiores a los obtenidos en los otros grupos.

(Sometido por Rafael Villavicencio, MD)





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**When painful spasm  
is the presenting  
symptom...**





...in the functional bowel/irritable bowel syndrome\*

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## (dicyclomine hydrochloride USP)

10 mg. capsules, 20 mg. tablets,  
10 mg./5 ml. syrup, 10 mg./ml. injection

helps control abnormal motor activity  
with minimal anticholinergic side effects†

### Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

*"The correlation of spasm relief and drug given was excellent."*

\*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

#### Reference:

King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

# Merrell



# Bentyl®

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Capsules, Tablets, Syrup, Injection

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective:

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

**CONTRAINDICATIONS:** Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient; unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis; toxic megacolon complicating ulcerative colitis, myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur.

**ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia; urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSEAGE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

**Usual Dosage:** Bentyl 10 mg capsule and syrup: *Adults:* 1 or 2 capsules or teaspoonfuls syrup three or four times daily. *Children:* 1 capsule or teaspoonful syrup three or four times daily. *Infants:* ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg: *Adults:* 1 tablet three or four times daily. Bentyl Injection: *Adults:* 2 ml (20 mg) every four to six hours intramuscularly only. **NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine® (bethanecol chloride USP) should be used.

Product Information as of October, 1978.

Injectable dosage forms manufactured by CONNAUGHT LABORATORIES, INC., Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Ocaturo, Illinois 62525 or MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215, U.S.A.

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January 14-18, 1980

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To apply: Registration Secretary, Extramural Programs Department, American College of Cardiology, 9111 Old Georgetown Road, Bethesda, Md. 20014.

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**CORONARY, HYPERTENSIVE, VALVULAR AND MYOCARDIAL HEART DISEASES: The Multi-disciplinary Approach**

December 2-5, 1979

Program Director:  
William C. Roberts, MD, FACC

To be presented at: The Williamsburg Conference Center, Williamsburg Lodge, Williamsburg, Virginia.

To apply: Registration Secretary, Extramural Programs Department, American College of Cardiology, 9111 Old Georgetown Road, Bethesda, Md. 20014.

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**SPORTSMEDICINE IN RURAL SCHOOLS** This course

will cover such aspects of sportsmedicine as pre-season testing for various sports related to classic injury sites and positive recuperation programs, highlighting some specific programs. It will also cover the basic guidelines for the team physician in establishing an advance plan for handling injuries. (60 minutes).

Instructor: J. M. Ingalls, MD  
Paris Community Hospital  
Paris, Illinois

**PLASTIC WOUND CLOSURE TECHNIQUES FOR THE PRIMARY CARE PHYSICIAN** This course will train physicians in general principles of wound closures, use of simple flaps, grapples and Z-plastys, dressing and management of post-operative wounds. Biological material will be provided. (120 minutes).

Instructor: William M. Champion, MD  
Plastic Surgery Associates, Inc.  
Seattle, Washington

**NUTRITIONAL ASSESSMENT AND MANAGEMENT IN RURAL AREAS** This course will cover proper treatment of malnutrition, often a major unrecognized symptom of illness, including routine surveillance and nutritional history. The course will deal specifically with techniques and concepts regarding the incorporation of nutritional therapy into the physician's practice. (60 minutes)

Instructor: George Blackburn, MD  
New England Deaconess Hospital  
Boston, Massachusetts

**AGRICULTURAL HEALTH PROBLEMS** This will consist of two special workshops in the area of agricultural zoonoses.

Workshop I - Occupational health hazards relative to contact with dairy cattle, beef cattle, and sheep. (120 minutes).

Workshop II - Occupational health hazards relative to contact with poultry, swine and the agricultural environment. (120 Minutes).

Instructor: Kelley J. Donham, D. V. M.  
Institute of Agricultural Medicine, Department of Preventive Medicine and Environmental Health, University of Iowa College of Medicine, Iowa City, Iowa.

**PRIMARY MANAGEMENT OF SEVERE HEAD TRAUMA** This program will concentrate on primary care of acute head injuries stressing recognition of acute and emergent problems, techniques of decompression and stabilizing for transportation. (120 minutes).

Instructor: David G. Piepgras, MD  
Department of Neurologic Surgery  
Mayo Clinic  
Rochester, Minnesota

**HAND AMPUTATION: HOW TO HELP A PATIENT**

**AND MICROSURGEON** This program will provide an introduction to microsurgery with follow-up in five areas: (60 minutes)

Basic Science - Vascular anatomy, nerve anatomy, surgical alterations

Free Tissue Transfer- Free flap transfer, toe to hand transfer

Instructor: Allen Van Beek, MD  
Division of Plastic Surgery  
Section of Microsurgery  
Southern Illinois University School of Medicine  
Springfield, Illinois

Sponsors of the Rural Health Conference, with the American Medical Association, are the American Hospital Association's Center for Small or Rural Hospitals, the American Nurses Association, the American Pharmaceutical Association, the Cooperative Extension Service of the United States Department of Agriculture, the Farm Foundation, the Massachusetts Medical Society and the National Safety Council.

Physicians wishing further information about the course schedule should call Mrs. Chapman or Mr. Smith or write to the Department of Community Health Systems, American Medical Association, 535 North Dearborn Street, Chicago, Illinois 60610.



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ointment may be used to prevent bacterial contamination in burns, skin grafts, incisions, and other clean lesions. For abrasions, minor cuts and wounds accidentally incurred, its use may prevent the development of infection and permit wound healing.

**CONTRAINDICATIONS:** This product is contraindicated in those individuals who have shown hypersensitivity to any of its components. Do not use in the eyes or in the external ear canal if the eardrum is perforated.

**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control

secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

**PRECAUTIONS:** As with other antibacterial preparations, prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

**ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.

Each gram

contains: Aerosporin<sup>®</sup>

(Polymyxin B Sulfate) 5,000

units, bacitracin zinc 400 units, neomy-

cin sulfate 5 mg (equivalent to 3.5 mg neomycin

base), special white petrolatum qs; in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

**INDICATIONS:** *Therapeutically*, (as an adjunct to systemic therapy when indicated), for topical infections, primary or secondary, due to susceptible organisms, as in: infected burns, skin grafts, surgical incisions, otitis externa; primary pyodermas (impetigo, ecthyma, sycosis vulgaris, paronychia); secondarily infected dermatoses (eczema, herpes, and seborrheic dermatitis); traumatic lesions, inflamed or suppurating as a result of bacterial infection. *Prophylactically*, the

The functional bowel and  
other unexplained G.I. disturbances...

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## FOR LACTOSE INTOLERANCE

Most people gradually stop producing lactase, the milk sugar splitting enzyme, shortly after weaning. With the exception of most Northern Europeans, few ethnic groups handle lactose well, especially as adults. In fact, some groups such as adult Blacks, Orientals and American Indians seem to be almost without any ability to produce lactase. Central European and Mediterranean descendents clearly demonstrate the problem to a moderate degree.

Estimates vary, but there are believed to be some 30 million lactose intolerant persons in the U.S. alone.

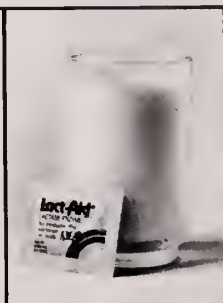
Therefore, lactose intolerance should be an immediate consideration when there are G.I. complaints of unknown etiology.

Suspect lactase deficiency when your patient complains of gas, indigestion, excessive flatulence, diarrhea or vague abdominal pain. Consider too, that a patient with known organic bowel disease may also have lactose-related problems.

- Q. Does all this mean that such patients must refrain from the use of milk and other dairy products?
- A. Probably not. One packet of Lact-Aid<sup>®</sup> properly mixed with one quart of milk provides sufficient lactase enzyme to hydrolyze most of the lactose into the simple sugars, galactose and glucose, for easy absorption. Two packets can effect quantitative conversion.

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## N O T I C I A S

### AMA NEWS:

#### *REPORTS OF PRODUCTS CAUSING CANCER HELD SOMETIMES PREMATURE, UNFOUNDED*

CHICAGO — Government agencies sometimes go off half-cocked in labeling foods and drugs as cancer causing, the editor of the Journal of the American Medical Association declares in an editorial in the Aug. 31 issue.

William R. Barclay, MD, calls for “a task force of editors of the major medical journals to respond quickly to prematurely issued reports, to challenge officials who promulgate those reports, and to advise science reporters on which of the reports are accurate, responsible, and acceptable.

“Allegations against artificial sweeteners, atomic energy plants, food colorings and preservatives, pharmaceutical products, and industrial chemicals are made almost daily, and keep the public in a state of fear that borders on hysteria,” Dr. Barclay charges.

“Tests that form the basis of these reports are often conducted with dosages that exceed any to which man could be exposed, are given by inappropriate routes, and are finally evaluated by persons of questionable expertise in the field of tumor histology.

“Many of the reports on carcinogenesis that have been made public have been flawed in both design and interpretation, but have been accepted by agencies that funded them, by the news media, and finally, by the public. Although ignorance of the existence of a hazard can be dangerous, false information can be even

more dangerous, and while one cannot quarrel with the concept of a fully informed public or defend science’s cloaking itself in secrecy, one can demand responsible evaluation and reporting of scientific data,” the Journal editor declares.

Dr. Barclay charges that sometimes those in government agencies who first receive a report and summarize it may have a preconceived bias against a drug. This may have been the case in the recent report that reserpine, a product widely prescribed to ease high blood pressure, causes cancer, he says. The summary report first released to the press was widely publicized. But the detailed report, not available until later, did not, “in our opinion, justify the conclusion that reserpine is carcinogenic.” There even was some evidence that the drug offers protection against tumors, rather than causing them, he points out.

“Scientific journals generally submit the information they receive to peer review and careful editing before publication. This helps to ensure a responsible degree of validity to both the findings and the conclusions.

“Unfortunately, the same degree of care has not been exercised when government agencies have released reports to the press. Reports are frequently issued at the end of the week, and several days then elapse before the information can be either verified or discounted. By that time the mischief has been done and is difficult to undo.

“It is incumbent on the government to exercise extreme care in the analysis of these studies, to submit the reports to careful scientific peer review, and to be



certain that any interpretation of the reports to the lay press accurately reflects conclusions that the data can support."

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### FINAL ELIMINATION OF MEASLES BY 1982 HELD ATTAINABLE GOAL

CHICAGO — The United States can eliminate measles by 1982, the Surgeon General of the United States declares in an editorial in the Sept. 14 Journal of the American Medical Association.

"I think the elimination of indigenous measles in this country is indeed a realistic goal," says Julius B. Richmond, MD, U. S. Surgeon General.

Dr. Richmond's editorial accompanies a study of the effort to eliminate measles by the Center for Disease Control, Atlanta. Alan R. Hinman, MD, and colleagues trace the efforts to halt measles in the past year and conclude that complete elimination in this country is feasible.

Levels of immunization already are quite high among American children and cases of measles have dropped sharply, Dr. Richmond points out. Of 46 states surveyed in the fall of 1978, he says, 29 reported that 90 per cent or more of children entering school for the first time had received measles vaccine. In 16 of these states the level was 95 percent.

Measles has been declining for 15 years, since the advent of the vaccine, and the public has tended to forget that the disease, while mild for most, still can cause complications leading to encephalitis, mental retardation, and even death, the Surgeon General points out.

It is feasible to vaccinate virtually all American children and to halt spread of infection within this nation, but there will continue to be frequent importations of measles from other countries, and it will be essential to maintain surveillance systems and immunization programs, the federal report says.

In 1978 there were 26,795 cases of measles reported, a decline of 53 per cent from the previous year. Three states, New Mexico, South Dakota and

Wyoming, were free of reported measles throughout the year. In the first 26 weeks of 1979 only 10,686 cases were reported, an all-time low.

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### SMOKING IS RULED OUT FOR WOMEN USING THE PILL

CHICAGO — Women who use oral contraceptives should not smoke cigarettes, says a report in the Sept. 14 Journal of the American Medical Association.

Cigarette smoking is an overwhelming risk factor for vascular disease in women, researchers found in the Kaiser-Permanente Contraceptive Drug Study, Walnut Creek, Cal.

Following more than 16,000 women for more than six years, the group determined that smoking significantly increases risk of heart attack, brain hemorrhage, other strokes and blood clots in the veins. Use of oral contraceptives by nonsmokers was associated with a moderate increase only in risk of brain hemorrhage and blood clots.

Use of noncontraceptive estrogens was not associated with increased risk of any of these diseases, the study found.

High blood pressure, high cholesterol, obesity, gallbladder disease and nondrinking of alcohol were all associated with increased risk of heart attack, whereas only high blood pressure and high cholesterol were associated with increased risk of other strokes.

The risk of vascular disease and strokes increases tremendously in women who both use oral contraceptives and smoke cigarettes.

Says Savitri Ramcharan, MD, of the Contraceptive Drug Study, in California:

"Smoking should be considered a contraindication to oral contraceptive use, or at the very least, women wishing to use oral contraceptives should be strongly urged not to smoke."

The researchers devised a Relative Risk scale to measure the impact of smoking on health. Smokers

have a relative risk of 2.9 for heart attacks, 5.7 for brain hemorrhage, 4.8 for other strokes, and 3.9 for blood clots. In oral contraceptive users who also smoked, relative risk of brain hemorrhage jumped to 21.9.

The Center for Disease Control at Atlanta joined the Kaiser-Permanente group in conducting the study, under the direction of Diana B. Petitti, MD.

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#### **LACK OF EXERCISE IS MINOR RISK FACTOR IN HEART ILLS**

CHICAGO — Lack of exercise increases a man's risk of heart disease, but not much. High blood pressure, smoking, overweight and high cholesterol are more dangerous risk factors.

These are the findings in the latest report from the Framingham Study, a longterm investigation into many aspects of heart disease. The report is in the August issue of an American Medical Association specialty journal, *Archives of Internal Medicine*.

William B. Kannel, MD, of Boston University School of Medicine, Framingham, Mass., tells of studies in which 1,909 men and 2,311 women were assessed for level of physical activity, and then observed for 14 years to determine how many suffered heart disease.

The effect of being sedentary on death rate is rather modest for men, compared to the effects of other risk factors. For women, the effect is negligible, Dr. Kannel says.

Active men live longer than sedentary ones, and have less heart disease, and the doctors by no means belittle the importance of regular exercises, either at work or at play or both.

But, "It has not yet been convincingly or consistently established that physical activity is an important determinant of the degree to which the major risk factors exist in the general population. In the Framingham Study, the correlations between physical activity and the major risk factors of systolic blood pressure, serum cholesterol level, and cigarette consumption are very small." Dr. Kannel reports.

#### **HYPERBARIC OXYGEN CHAMBER SUCCEEDS IN TREATING AIR BUBBLES IN BODY**

CHICAGO — A serious and common medical problem is the air bubble. Some 20,000 individuals each year suffer permanent brain damage from an air bubble that gets into the blood stream and reaches the brain.

Successful treatment of the air bubble, properly called air embolism, with use of a hyperbaric oxygen chamber is reported in the August issue of an American Medical Association specialty journal, *Archives of Neurology*.

Air emboli have been reported following an injury or surgery, from intravenous therapy, kidney dialysis, some diagnostic procedures requiring injections, oral genital sexual relations in the female, high altitude accidents, and diving accidents, says Jon T. Mader, MD, of the University of Texas Medical Branch, Galveston, Texas.

Conventional treatment heretofore has been unsatisfactory, resulting in a death rate of 30 per cent, Dr. Mader reports. But with hyperbaric oxygen chamber treatment, the death rate has been held down to 6 per cent.

The patient is placed in one of the large chambers designed originally by the U. S. Navy to aid in decompression of divers and submariners who surface too fast from a deep dive. Air pressure is greatly increased in the chamber.

Treatment is most effective when begun promptly, but can be of help even after a delay of up to 29 hours, Dr. Mader says. Pressure decreases the size of the bubbles. Inhaling 100 per cent oxygen clears nitrogen from the blood and accelerates absorption of air bubbles. Chamber treatment lowers pressure on the brain by half, and also results in more oxygen reaching brain tissues, he found.

Dr. Mader describes treatment of a 23-year old woman suffering from an air embolism. Recovery was excellent. Treatment was by a protocol developed by the Navy for treating air embolism occurring in submarine escape training.

*American College of Emergency Physicians*

Perforation of the esophagus due to ingestion of a round, smooth foreign object is rare. However, a 16-month-old child who swallowed an alkaline battery suffered perforation of the esophagus, and subsequently the aorta, with fatal results.

In a case report published in the September issue of the *Journal of the American College of Emergency Physicians* and the *University Association for Emergency Medicine (JACEP)*, Charles L. Shabino, MD, FAAP, and Arthur N. Feinberg, MD, FAAP, discuss the unusual complications of a common occurrence: children swallowing coin-shaped or round objects. Dr. Shabino is director of the Pediatric Intensive Care Unit of Bronson Methodist Hospital in Kalamazoo, Michigan, where Dr. Feinberg also practices.

Children often swallow foreign bodies, most of which pass through the alimentary tract without lodging in the esophagus. Once an object is lodged, however, the esophagus, unlike the stomach or intestinal tract, does not have the strength to peristaltically expel the matter, the article explains.

According to the report, "Esophageal Perforation Secondary to Alkaline battery Ingestion", the alkaline battery, entrapped for three days, chemically burned through the esophagus and aortic arch causing internal bleeding and cardiac arrest. The symptoms had been irritability, vomiting, rapid breathing and slight fever.

"Parents should be aware of the potential danger of small objects in the hands of an infant," Dr. Shabino said. "The incidence of young patients in the emergency department who have swallowed a coin, pieces of a toy, and so forth is high. It should be stressed that while many of these objects will normally pass through the child's digestive system, an alkaline battery possesses chemical properties which

make it imperative the battery is removed immediately.

---

If a person walks into the emergency department with a gunshot or stab wound, chances are the patient is an unmarried male between 16 and 30 years of age.

This conclusion is offered by R. Edward Wase, Jr., MD, and Harold F. Hamit, MD, who studied "Socioeconomic Aspects of Stab and Gunshot Wounds" at Charlotte Memorial Hospital and Medical Center in Charlotte, North Carolina. Records of 294 patients with gunshot and stab wounds admitted to that hospital between July 1, 1976 and June 30, 1977 were reviewed, and results are published in the September issue of the *Journal of the American College of Emergency Physicians* and the *University Association for Emergency Medicine (JACEP)*.

Patterns developed in some of the 24 clinical, social and economic aspects studied. For instance: 83 percent of the patients were male; 56 percent were between 16 and 30; 45 percent were single (compared to 30 percent married, 15 percent separated, 7 percent divorced, and 2 percent widowed); 55 percent of the patients arrived at the hospital between 10:00 pm and 3:00 am, and approximately 57 percent arrived on Friday, Saturday, or Sunday.

Hospital costs generated by these patients are most often picked up by the taxpayer, according to the study.

"The number of patients admitted to Charlotte Memorial Hospital and Medical Center with injuries from stabbings and gunshot and shotgun wounds has increased in the last ten years. We have discovered some patterns, but we desperately need assistance from lawmakers and sociologists in combating these apparently preventable injuries," Dr. Wase said.



## Instrucciones para los Autores

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

**Manuscrito:** El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos a maquinilla a doble espacio y por un solo lado de cada página, en **TRIPLICADO** y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

**Nomenclatura:** Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

**Tablas:** Las tablas deben aparecer en hojas separadas. Estas deben incluir el título y el número de la tabla (romano). Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla.

**Figuras:** Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor y debe indicarse la parte superior.

**Referencias:** Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Estas deben seguir el estilo o patrón del "Index Medicus", el cual se describe a continuación:

### Para artículos de Revista:

Apellido(s), e iniciales del autor(es), nombre de la revista, volumen, primera página y año.

Koppisch E.: Bol Asoc Med P Rico 46: 505, 1954.

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Wintrobe MM: Clinical Hematology, 3rd Ed Lea and Febiger, Philadelphia 1952 p. 67.

Más de tres autores añadir: et al.

Deben usarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana.

Como guía de referencia para preparar su artículo puede usar la publicación Advice to Authors que publica la Scientific Publications Division, American Medical Association, 535 N Dearborn Street, Chicago, Illinois, 60610.

## Instructions to Authors

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the

understanding that it is to be published solely in this journal.

In order to facilitate review of the article by the Editorial Board and the work of the printer, the authors must conform with the following instructions:

**Manuscripts:** The entire manuscript, including legends and references should be typewritten double spaced in *TRIPLICATE* with ample margins. A separate title page should include the following: title, authors and their degrees (e.g. MD, FACP), city where the work was done, hospital or academic institutions, acknowledgment of financial sponsors, and if the paper has been presented at a meeting the place and date should be given.

The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

**Nomenclature:** Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurements should be used preferentially.

**Tables:** These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines

should be omitted.

**Figures:** Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

**References:** These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text. This list should conform to the Style of the Index Medicus and should be punctuated as in the following examples.

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Wintrobe MM: *Clinical Hematology*, 3rd Ed Lea and Febiger, Philadelphia 1952 p 67.

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# Enterococcus:

## One reason for failure...

It is well known that *Escherichia coli* causes most cases of UTI. Enterococcus (also called *Streptococcus faecalis* and *Streptococcus*, group D) has become the second most prevalent uropathogen<sup>1,2</sup>—particularly in sexually active women.<sup>3</sup>

**MACRODANTIN** offers superior in vitro<sup>\*</sup> efficacy against these pathogens: 96% against *E. coli*... 94% against enterococcus.

<sup>\*</sup>In vitro data do not necessarily predict clinical efficacy.

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capsules: 25 mg, 50 mg, 100 mg  
**Macrodan<sup>®</sup>**  
(nitrofurantoin macrocrystals)

Macrodan is indicated for the treatment of urinary tract infections when due to susceptible strains of *Escherichia coli*, enterococci, *Staphylococcus* species (it is not indicated for the treatment of associated renal cortical or perinephric abscesses), and certain susceptible strains of *Klebsiella* species, *Enterobacter* species, and *Proteus* species.

**NOTE:** Specimens for culture and susceptibility testing should be obtained prior to and during drug administration.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function (creatinine clearance under 40 ml per minute) are contraindications to therapy with this drug. Treatment of this type of patient carries an increased risk of toxicity because of impaired excretion of the drug. For the same reason, this drug is much less effective under these circumstances.

The drug is contraindicated in pregnant patients at term as well as in infants under one month of age because of the possibility of hemolytic anemia due to immature enzyme systems (glutathione instability).

The drug is also contraindicated in those patients with known hypersensitivity to Macrodan, Furadantin<sup>®</sup> (nitrofurantoin), and other nitrofurantoin preparations.

**WARNINGS:** Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin products. If these reactions occur, the drug should be withdrawn and appropriate measures should be taken.

An insidious onset of pulmonary reactions (diffuse interstitial pneumonitis or pulmonary fibrosis, or both) in patients on long-term therapy warrants close monitoring of these patients.

There have been isolated reports giving pulmonary reactions as a contributing cause of death. (See Hypersensitivity reactions.)

Cases of hemolytic anemia of the primaquine sensitivity type have been induced by Macrodan. The hemolysis appears to be linked to a glucose-6-phosphate dehydrogenase deficiency in the red blood cells of the affected patients. This deficiency is found in 10 percent of Negroes and a small percentage of ethnic groups of Mediterranean and Near-Eastern origin. Any sign of hemolysis is an indication to discontinue the drug. Hemolysis ceases when the drug is withdrawn.

*Pseudomonas* is the organism most commonly implicated in superinfections in patients treated with Macrodan.

**PRECAUTIONS:** Peripheral neuropathy may occur with Macrodan therapy; this may become severe or irreversible. Fatalities have been reported. Predisposing conditions such as renal impairment (creatinine clearance under 40 ml per minute), anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**Usage in Pregnancy:** The safety of Macrodan during pregnancy and lactation has not been established. Use of this drug in women of childbearing potential requires that the anticipated benefit be weighed against the possible risks.

**ADVERSE REACTIONS:** **Gastrointestinal reactions:** Anorexia, nausea and emesis are the most frequent reactions; abdominal pain and diarrhea occur less frequently. These dose-related toxicity reactions can be minimized by reduction of dosage, especially in the female patient. Hepatitis occurs rarely.

**Hypersensitivity reactions:** Pulmonary sensitivity reactions may occur, which can be acute, subacute, or chronic.

Acute reactions are commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution may be dramatic.

In subacute reactions, fever and eosinophilia are observed less often. Recovery is somewhat slower, perhaps as long as several months. If the symptoms are not recognized as being drug related and nitrofurantoin is not withdrawn, symptoms may become more severe.

Chronic pulmonary reactions are more likely to occur in patients who have been on continuous nitrofurantoin therapy for six months or longer. The insidious onset of malaise, dyspnea on exertion, cough, and altered pulmonary function are common manifestations. Roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis, or both, are also common manifestations. Fever is rarely prominent.

The severity of these chronic pulmonary reactions and the degree of their resolution appear to be related to the duration of

therapy after the first clinical signs appear. Pulmonary function may be permanently impaired even after cessation of nitrofurantoin therapy. This risk is greater when pulmonary reactions are not recognized early.

**Dermatologic reactions:** Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other sensitivity reactions:** Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and arthralgia.

**Hematologic reactions:** Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

**Neurological reactions:** Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

**Miscellaneous reactions:** Transient alopecia. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrodan, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

**References:** 1. Center for Disease Control: *National Nosocomial Infections Study Report*, Annual Summary 1976, issued February 1978. Washington, DC, U.S. Department of Health, Education, and Welfare, p 8. 2. Cooper J, et al: Diagnostic and chemoprophylactic importance of perineal microbial carriage, in Siegenthaler W, Luthy R (eds): *Current Chemotherapy*. Washington, DC, American Society for Microbiology, 1978, vol 1, pp 198-200. 3. Buckley RM, McGuckin M, MacGregor RR: Urine bacterial counts after sexual intercourse. *N Engl J Med* 298:321-324, 1978. 4. PMR Bacteriologic Report, Summer Series, 1978; a national bacteriologic monitoring service for 200 acute-care hospitals of 100 beds or more.

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# All clear in Miami

Ordinary topical corticosteroids are generally not recommended when infection complicates dermatoses.\* That's why your patients need Vioform®Hydrocortisone.

Because Vioform-Hydrocortisone provides four-way action in just one preparation—antibacterial and antifungal, as well as antipruritic and anti-inflammatory actions. Think of it first for thorough, fast clearing of skin problems on Miami...or on any beach.

This drug has been evaluated as possibly effective for these indications

## Vioform®Hydrocortisone (iodochlorhydroxyquin and hydrocortisone)

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences-National Research Council and/or other information, FDA has classified the indications as follows:

**"Possibly" effective:** Contact or atopic dermatitis, impetiginized eczema, nummular eczema, infantile eczema, endogenous chronic infectious dermatitis, stasis dermatitis, pyoderma, nuchal eczema and chronic eczematoid otitis externa, acne urticata, localized or disseminated neurodermatitis, lichen simplex chronicus, anogenital pruritus (vulvae, scroti, ani), folliculitis, bacterial dermatoses, mycotic dermatoses such as tinea (capitis, cruris, corporis, pedis), moniliasis, intertrigo.

Final classification of the less-than-effective indications requires further investigation

### CONTRAINDICATIONS

Hypersensitivity to Vioform-Hydrocortisone, or any of its ingredients or related compounds, lesions of the eye, tuberculosis of the skin, most viral skin lesions (including herpes simplex, varicella, varicella)

### WARNINGS

*This product is not for ophthalmic use*

In the presence of systemic infections, appropriate systemic antibiotics should be used

### Usage in Pregnancy

Although topical steroids have not been reported to have an adverse effect on pregnancy, the safety of their use in pregnant women has not been absolutely established. In laboratory animals, increases in incidence of fetal abnormalities have been associated with exposure of gestating females to topical corticosteroids in some cases at rather low dosage levels. Therefore, drugs of this class should not be used extensively on pregnant patients in large amounts or for prolonged periods of time

### PRECAUTIONS

May prove irritating to sensitized skin in rare cases. If irritation occurs, discontinue therapy. Staining may occur.

Signs and symptoms of systemic toxicity, electrolyte imbalance, or adrenal suppression have not been reported with Vioform-Hydrocortisone. Nevertheless, the possibility of suppression of the pituitary-adrenal axis during therapy should be kept in mind, especially when the drug is used under occlusive dressings, for a prolonged period or for treating extensive cutaneous areas. Since significant absorption of corticosteroid may occur under these conditions, particularly in children and infants.

Vioform may be absorbed through the skin and interfere with thyroid function tests. If such tests are contemplated, wait at least one month between discontinuation of therapy and performance of these tests. The ferric chloride test for phenylketonuria (PKU) can yield a false-positive result if Vioform is present in the diaper or urine. Prolonged use may result in overgrowth of non-susceptible organisms requiring appropriate therapy.

### ADVERSE REACTIONS

There have been a few reports of rash and hypersensitivity. The following local adverse reactions have been reported with topical corticosteroids, especially under occlusive dressings: burning, itching, irritation, dryness, folliculitis, hypertrichosis, acneiform eruptions, hypopigmentation, perioral dermatitis, allergic contact dermatitis, maceration of the skin, secondary infection, skin

atrophy, striae, milium. Discontinue therapy if any untoward reaction occurs.

### DOSEAGE AND ADMINISTRATION

Apply a thin layer to the affected parts 3 or 4 times daily.

The Cream, because of its slight drying effect, is primarily useful for moist, weeping lesions; the Lotion is particularly suitable for application behind the ears and in intertriginous areas of the body; the Ointment is best used for dry lesions accompanied by thickening and scaling of the skin.

The Mild Cream and Mild Ointment should be used when treating lesions involving extensive body areas or less severe dermatoses.

### HOW SUPPLIED

Cream, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water, tubes of 5 and 20 Gm.

Ointment, 3% iodochlorhydroxyquin and 1% hydrocortisone in a petrolatum base, tubes of 20 Gm.

Lotion, 3% iodochlorhydroxyquin and 1% hydrocortisone in a water-washable base containing stearic acid, cetyl alcohol, lanolin, propylene glycol, sorbitan trioleate, polysorbate 60, triethanolamine, methylparaben, propylparaben, and perfume Flora in water, plastic squeeze bottles of 15 ml.

Mild Cream, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a water-washable base containing stearyl alcohol, cetyl alcohol, stearic acid, petrolatum, sodium lauryl sulfate, and glycerin in water, tubes of 1/2 and 1 ounce.

Mild Ointment, 3% iodochlorhydroxyquin and 0.5% hydrocortisone in a petrolatum base, tubes of 1 ounce.

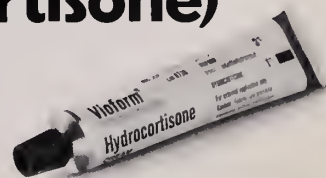
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**Plus** MAGNESIUM  
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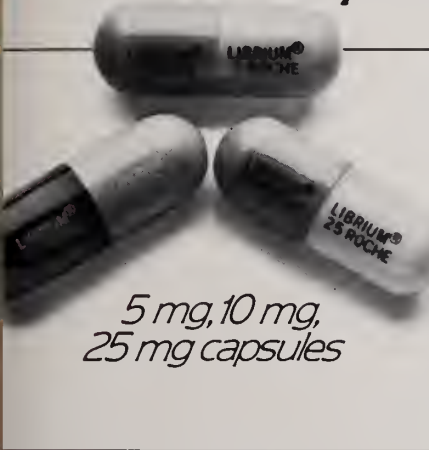


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# *Librium*<sup>®</sup>

## *chlordiazepoxide HCl/Roche*



- ☐ Proven antianxiety performance
- ☐ An unsurpassed safety record
- ☐ Predictable patient response
- ☐ Minimal effect on mental acuity at recommended doses
- ☐ Minimal interference with many primary medications, such as antacids, anticholinergics, diuretics, cardiac glycosides and antihypertensive agents

Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** Relief of anxiety and tension occurring alone or accompanying various disease states. Efficacy beyond four months not established by systematic clinical studies. Periodic reassessment of therapy recommended.

**Contraindications:** Patients with known hypersensitivity to the drug.

**Warnings:** Warn patients that mental and/or physical abilities required for tasks such as driving or operating machinery may be impaired, as may be mental alertness in children, and that concomitant use with alcohol or CNS depressants may have an additive effect. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and

acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

**Adverse Reactions:** Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

**Usual Daily Dosage:** Individualize for maximum beneficial effects. Oral—Adults: Mild and moderate anxiety and tension, 5 or 10 mg t.i.d. or q.i.d.; severe states, 20 or 25 mg t.i.d. or q.i.d. Geriatric patients: 5 mg b.i.d. to q.i.d. (See Precautions.)

**Supplied:** Librium<sup>®</sup> (chlordiazepoxide HCl) Capsules, 5 mg, 10 mg and 25 mg—bottles of 100 and 500; Tel-E-Dose<sup>®</sup> packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10. Libritabs<sup>®</sup> (chlordiazepoxide) Tablets, 5 mg, 10 mg and 25 mg—bottles of 100 and 500. With respect to clinical activity, capsules and tablets are indistinguishable.

*synonymous  
with relief of anxiety*

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Please see following page.

# *Librium*®

*chlordiazepoxide HCl/Roche*  
*5 mg, 10 mg, 25 mg capsules*



*synonymous*  
*with relief of anxiety*

ROCHE

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# BOLETIN

ASOCIACION MEDICA DE PUERTO RICO

C O N T E N I D O

JAN 7 1980

UPDATE ON SARCOIDOSIS

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THE USE OF FROZEN SEMEN FOR ARTIFICIAL INSEMINATION

EDITORIAL: EDUCACION MEDICA EN PUERTO RICO

CARTA AL EDITOR: LA REGIONALIZACION MEDICA EN PUERTO RICO

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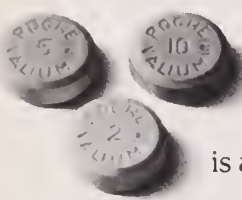
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# A character all its own.



Valium (diazepam/Roche)  
is a benzodiazepine with a  
character all its own.

Pharmacologically, it is a potent skeletal muscle relaxant and anticonvulsant (in adjunctive use), as well as an antianxiety agent. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

**Valium<sup>®</sup> IV**  
**diazepam/Roche**  
2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

**Dosage:** Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

**Supplied:** Valium<sup>®</sup> (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose<sup>®</sup> packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.



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# Enterococcus:

## One reason for failure...

It is well known that *Escherichia coli* causes most cases of UTI. Enterococcus (also called *Streptococcus faecalis* and *Streptococcus*, group D) has become the second most prevalent uropathogen<sup>1,2</sup>—particularly in sexually active women.<sup>3</sup>

**MACRODANTIN** offers superior in vitro\* efficacy against these pathogens: 96% against *E. coli*...  
94% against enterococcus.

\*In vitro data do not necessarily predict clinical efficacy.

...reason enough to choose

capsules: 25 mg 50 mg 100 mg  
**Macrochantin<sup>®</sup>**  
(nitrofurantoin macrocrystals)

**INDICATIONS:** Macrochantin is indicated for the treatment of urinary tract infections when due to susceptible strains of *Escherichia coli*, enterococci, *Staphylococcus aureus* (it is not indicated for the treatment of associated renal, cortical or perinephric abscesses), and certain susceptible strains of *Klebsiella* species, *Enterobacter* species, and *Proteus* species.

**NOTE:** Specimens for culture and susceptibility testing should be obtained prior to and during drug administration.

**CONTRAINDICATIONS:** Anuria, oliguria, or significant impairment of renal function (creatinine clearance under 40 ml per minute) are contraindications to therapy with this drug. Treatment of this type of patient carries an increased risk of toxicity because of impaired excretion of the drug. For the same reason, this drug is much less effective under these circumstances.

The drug is contraindicated in pregnant patients at term as well as in infants under one month of age because of the possibility of hemolytic anemia due to immature enzyme systems (glutathione instability).

The drug is also contraindicated in those patients with known hypersensitivity to Macrochantin, Furadantin<sup>®</sup> (nitrofurantoin), and other nitrofurantoin preparations.

**WARNINGS:** Acute, subacute and chronic pulmonary reactions have been observed in patients treated with nitrofurantoin products. If these reactions occur, the drug should be withdrawn and appropriate measures should be taken.

An insidious onset of pulmonary reactions (diffuse interstitial pneumonitis or pulmonary fibrosis, or both) in patients on long-term therapy warrants close monitoring of these patients.

There have been isolated reports giving pulmonary reactions as a contributing cause of death. (See Hypersensitivity reactions.)

Cases of hemolytic anemia of the primaquine sensitivity type have been induced by Macrochantin. The hemolysis appears to be linked to a glucose-6-phosphate dehydrogenase deficiency in the red blood cells of the affected patients. This deficiency is found in 10 percent of Negroes and a small percentage of ethnic groups of Mediterranean and Near-Eastern origin. Any sign of hemolysis is an indication to discontinue the drug. Hemolysis ceases when the drug is withdrawn.

*Pseudomonas* is the organism most commonly implicated in superinfections in patients treated with Macrochantin.

**PRECAUTIONS:** Peripheral neuropathy may occur with Macrochantin therapy; this may become severe or irreversible. Fatalities have been reported. Predisposing conditions such as renal impairment (creatinine clearance under 40 ml per minute), anemia, diabetes, electrolyte imbalance, vitamin B deficiency, and debilitating disease may enhance such occurrence.

**Usage in Pregnancy:** The safety of Macrochantin during pregnancy and lactation has not been established. Use of this drug in women of childbearing potential requires that the anticipated benefit be weighed against the possible risks.

**ADVERSE REACTIONS:** **Gastrointestinal reactions:** Anorexia, nausea and emesis are the most frequent reactions; abdominal pain and diarrhea occur less frequently. These dose-related toxicity reactions can be minimized by reduction of dosage, especially in the female patient. Hepatitis occurs rarely.

**Hypersensitivity reactions:** Pulmonary sensitivity reactions may occur, which can be acute, subacute, or chronic.

Acute reactions are commonly manifested by fever, chills, cough, chest pain, dyspnea, pulmonary infiltration with consolidation or pleural effusion on x-ray, and eosinophilia. The acute reactions usually occur within the first week of treatment and are reversible with cessation of therapy. Resolution may be dramatic.

In subacute reactions, fever and eosinophilia are observed less often. Recovery is somewhat slower, perhaps as long as several months. If the symptoms are not recognized as being drug related and nitrofurantoin is not withdrawn, symptoms may become more severe.

Chronic pulmonary reactions are more likely to occur in patients who have been on continuous nitrofurantoin therapy for six months or longer. The insidious onset of malaise, dyspnea on exertion, cough, and altered pulmonary function are common manifestations. Roentgenographic and histologic findings of diffuse interstitial pneumonitis or fibrosis, or both, are also common manifestations. Fever is rarely prominent.

The severity of these chronic pulmonary reactions and the degree of their resolution appear to be related to the duration of

therapy after the first clinical signs appear. Pulmonary function may be permanently impaired even after cessation of nitrofurantoin therapy. This risk is greater when pulmonary reactions are not recognized early.

**Dermatologic reactions:** Maculopapular, erythematous, or eczematous eruption, pruritus, urticaria, and angioedema.

**Other sensitivity reactions:** Anaphylaxis, asthmatic attack in patients with history of asthma, cholestatic jaundice, drug fever, and arthralgia.

**Hematologic reactions:** Hemolytic anemia, granulocytopenia, leukopenia, eosinophilia, and megaloblastic anemia. Return of the blood picture to normal has followed cessation of therapy.

**Neurological reactions:** Peripheral neuropathy, headache, dizziness, nystagmus, and drowsiness.

**Miscellaneous reactions:** Transient alopecia. As with other antimicrobial agents, superinfections by resistant organisms may occur. With Macrochantin, however, these are limited to the genitourinary tract because suppression of normal bacterial flora elsewhere in the body does not occur.

**References:** 1. Center for Disease Control: *National Nosocomial Infections Study Report*, Annual Summary 1976, issued February 1978. Washington, DC, U.S. Department of Health, Education, and Welfare, p 8. 2. Cooper J, et al: Diagnostic and chemoprophylactic importance of perineal microbial carriage, in Siegenthaler W, Luthy R (eds): *Current Chemotherapy*. Washington, DC, American Society for Microbiology, 1978, vol 1, pp 198-200. 3. Buckley RM, McGuckin M, MacGregor RR: Urine bacterial counts after sexual intercourse. *N Engl J Med* 298:321-324, 1978. 4. PMR Bacteriologic Report, Summer Series, 1978; a national bacteriologic monitoring service for 200 acute-care hospitals of 100 beds or more.

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**Indication:** Hypertension. (See box warning.)

**Contraindications:** Mental depression, hypersensitivity, and most cases of severe renal or hepatic diseases.

#### Warnings:

These fixed combination drugs are not indicated for initial therapy of hypertension. Hypertension requires therapy titrated to the individual patient. If the fixed combination represents the dosage so determined, its use may be more convenient in patient management. The treatment of hypertension is not static, but must be reevaluated as conditions in each patient warrant.

Use with caution in patients with severe renal disease, impaired hepatic function or progressive liver disease. Regroton or Demi-Regroton may potentiate action of other antihypertensive, ganglionic and peripheral adrenergic-blocking drugs. Sensitivity reactions may occur in allergic and asthmatic patients. Discontinue one week before electroshock therapy, and if depression or peptic ulcer occurs. *Use in pregnancy:* Thiazides cross the placental barrier and appear in cord blood. The use of chlorthalidone and related drugs in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. Use with care in nursing mothers since thiazides and reserpine cross the placental barrier and appear in cord blood and breast milk. Increased respiratory secretions, nasal congestion, cyanosis and anorexia may occur in infants born to reserpine-treated

mothers. If use of the drug is essential, the patient should stop nursing. **Precautions:** Antihypertensive therapy with these drugs should always be initiated cautiously in postsympathectomy patients and in patients receiving ganglionic blocking agents, other potent antihypertensive drugs or curare. Reduce dosage of concomitant antihypertensive agents by at least one-half. To avoid hypotension during surgery, discontinue therapy with these agents two weeks prior to elective surgical procedures. In emergency surgery, use anticholinergic or adrenergic drugs or other supportive measures if needed. Because of the possibility of progression of renal damage, periodic kidney function tests are indicated. Discontinue if the BUN rises or liver dysfunction is aggravated (hepatic coma may be precipitated). Patients receiving chlorthalidone should have periodic determination of serum electrolytes and should be observed for clinical signs of fluid or electrolyte imbalance (hyponatremia, hypochloremic alkalosis and hypokalemia), particularly if they are receiving digitalis, parenteral fluids, or are vomiting excessively. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may decrease arterial responsiveness to

norepinephrine. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance. Use cautiously in patients with ulcerative colitis or gallstones (biliary colic may be precipitated). Bronchial asthma may occur in susceptible patients. **Adverse Reactions:** These drugs are generally well tolerated. The most frequent adverse reactions are anorexia, nausea, vomiting, gastric irritation, diarrhea, constipation, headache, dizziness, weakness, muscle cramps, nasal congestion, drowsiness and mental depression. Other potential side effects include skin rash, urticaria, ecchymosis; hyperglycemia and glycosuria (diabetics should be checked regularly), hyperuricemia and acute gout, and impotence. With chlorthalidone: restlessness, transient myopia; dysuria, orthostatic hypotension (may be potentiated by alcohol, barbiturates or narcotics), rare idiosyncratic reactions such as aplastic anemia, leukopenia, thrombocytopenia, agranulocytosis, purpura, necrotizing angitis and Lyell's syndrome (toxic epidermal necrolysis); pancreatitis when epigastric pain or unexplained G.I. symptoms develop after prolonged administration; other reactions reported with this class of compounds include jaundice, xanthopsia, paresthesia, and photosensitization. With reserpine: angina pectoris, bradycardia, ectopic cardiac rhythms (especially with digitalis); blurred vision, conjunctival injection, uveitis, optic atrophy, glaucoma, deafness, increased gastric secretions, dull sensorium, paradoxical anxiety, nightmares, reversible paralysis agitans syndrome, dyspnea, weight gain, dryness of mouth, increased susceptibility to colds, decreased libido, skin flushing and pruritus. **Dosage:** Should be determined by individual titration. (See box warning.) Dosage of either Regroton or Demi-Regroton for most patients is one tablet once a day. **How Supplied:** Regroton as pink, round, single-scored tablets in bottles of 100 and 1000; Demi-Regroton as white, round tablets, bottles of 100.





A reminder

# ZYLOPRIM® (allopurinol)

100 and 300 mg scored Tablets

- inhibits uric acid formation
- helps prevent urate crystal depositions in synovia
- reduces risk of uric acid lithiasis

**INDICATIONS AND USE:** This is not an innocuous drug and strict attention should be given to the indications for its use. Pending further investigation, its use in other hyperuricemic states is not indicated at this time.

Zyloprim® (allopurinol) is intended for:

1. treatment of gout, either primary, or secondary to the hyperuricemia associated with blood dyscrasias and their therapy;
2. treatment of primary or secondary uric acid nephropathy, with or without accompanying symptoms of gout;
3. treatment of patients with recurrent uric acid stone formation;
4. prophylactic treatment to prevent tissue urate deposition, renal calculi, or uric acid nephropathy in patients with leukemias, lymphomas and malignancies who are receiving cancer chemotherapy with its resultant elevating effect on serum uric acid levels.

**CONTRAINDICATIONS:** Use in children with the exception of those with hyperuricemia secondary to malignancy. The drug should not be employed in nursing mothers.

**Patients who have developed a severe reaction to Zyloprim should not be restarted on the drug.**

**WARNINGS:** ZYLOPRIM SHOULD BE DISCONTINUED AT THE FIRST APPEARANCE OF SKIN RASH OR ANY SIGN OF ADVERSE REACTION. In some instances a skin rash may be followed by more severe hypersensitivity reactions such as exfoliative, urticarial and purpuric lesions as well as Stevens-Johnson syndrome (erythema multiforme) and very rarely a generalized vasculitis which may lead to irreversible hepatotoxicity and death.

A few cases of reversible clinical hepatotoxicity have been noted and in some patients asymptomatic rises in serum alkaline phosphatase or serum transaminase have been observed. Accordingly, periodic liver function tests should be performed during the early stages of therapy, particularly in patients with pre-existing liver disease. Patients should be alerted to the need for due precautions when engaging in activities where alertness is mandatory.

Nevertheless, iron salts should not be given simultaneously with Zyloprim. This drug should not be administered to immediate relatives of patients with idiopathic hemochromatosis.

**In patients receiving Purlinethol® (mercaptopyrine) or Imuran® (azathioprine), the concomitant administration of 300-600 mg of Zyloprim per day will require a reduction in dose to approximately one-third to one-fourth of the usual dose of mercaptopyrine or azathioprine. Subsequent adjustment of doses of Purlinethol or Imuran should be made on the basis of therapeutic response and any toxic effects.**

**Usage in Pregnancy and Women of Childbearing Age:** Zyloprim® (allopurinol) should be used in pregnant women or women of childbearing age only if the potential benefits to the patient are weighed against the possible risk to the fetus.

**PRECAUTIONS:** Some investigators have reported an increase in acute attacks of gout during the early stages of allopurinol administration, even when normal or sub-normal serum uric acid levels have been attained.

It has been reported that allopurinol prolongs the half-life of the anticoagulant, dicumarol. This interaction should be kept in mind when allopurinol is given to patients already on anticoagulant therapy, and the coagulation time should be reassessed.

A fluid intake sufficient to yield a daily urinary output of at least 2 liters and the maintenance of a neutral or, preferably, slightly alkaline urine are desirable to (1) avoid the theoretic possibility of formation of xanthine calculi under the influence of Zyloprim therapy and (2) help prevent renal precipitation of urates in patients receiving concomitant uricosuric agents.

Patients with impaired renal function require less drug and should be carefully observed during the early stages of Zyloprim administration and the drug withdrawn if increased abnormalities in renal function appear.

In patients with severely impaired renal function, or decreased urate clearance, the half-life of oxipurinol in the plasma is greatly prolonged. Therefore, a dose of 100 mg per day or 300 mg twice a week, or perhaps less, may be sufficient to maintain adequate xanthine oxidase inhibition to reduce serum urate levels. Such patients should be treated with the lowest effective dose, in order to minimize side effects.

Mild reticulocytosis has appeared in some patients.

As with all new agents, periodic determination of liver and kidney function and complete blood counts should be performed especially during the first few months of therapy.

## ADVERSE REACTIONS:

**Dermatologic:** Because in some instances skin rash has been followed by severe hypersensitivity reactions, it is recommended that therapy be discontinued at the first sign of rash or other adverse reaction (see WARNINGS). Skin rash, usually maculopapular, is the adverse reaction most commonly reported.

Exfoliative, urticarial and purpuric lesions, Stevens-Johnson syndrome (erythema multiforme) and toxic epidermal necrolysis have also been reported.

A few cases of alopecia with and without accompanying dermatitis have been reported.

In some patients with a rash, restarting Zyloprim (allopurinol) therapy at lower doses has been accomplished without untoward incident.

**Gastrointestinal:** Nausea, vomiting, diarrhea, and intermittent abdominal pain have been reported.

**Vascular:** There have been rare instances of a generalized hypersensitivity vasculitis or necrotizing angiitis which have led to irreversible hepatotoxicity and death.

**Hematopoietic:** Agranulocytosis, anemia, aplastic anemia, bone marrow depression, leukopenia, pancytopenia and thrombocytopenia have been reported in patients, most of whom received concomitant drugs with potential for causing these reactions. Zyloprim® (allopurinol) has been neither implicated nor excluded as a cause of these reactions.

**Neurologic:** There have been a few reports of peripheral neuritis occurring while patients were taking Zyloprim. Drowsiness has also been reported in a few patients.

**Ophthalmic:** There have been a few reports of cataracts found in patients receiving Zyloprim. It is not known if the cataracts predated the Zyloprim therapy. "Toxic" cataracts were reported in one patient who also received an anti-inflammatory agent; again, the time of onset is unknown. In a group of patients followed by Gutman and Yü for up to five years on Zyloprim therapy, no evidence of ophthalmologic effect attributable to Zyloprim was reported.

**Drug Idiosyncrasy:** Symptoms suggestive of drug idiosyncrasy have been reported in a few patients. This was characterized by fever, chills, leukopenia or leukocytosis, eosinophilia, arthralgias, skin rash, pruritus, nausea and vomiting.

**OVERDOSAGE:** Massive overdosing, or acute poisoning, by Zyloprim has not been reported.

**HOW SUPPLIED:** 100 mg (white) scored tablets, bottles of 100 and 1000; 300 mg (peach) scored tablets, bottles of 30, 100 and 500. Unit dose packs for each strength also available.

Complete information available from your local B. W. Co. Representative or from Professional Services Department PML.

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- \* **Update on Sarcoidosis** ..... 325  
*D. Geraint James, MA, FRCP, MD and R. E. Figueroa Lebrón, MD, FCCP*

En este artículo James y Figueroa Lebrón resumen la información y trabajos presentados en la Octava Conferencia Internacional de Sarcoidosis celebrada en Londres en 1978. Los autores presentan y resumen los aspectos epidemiológicos, patológicos e inmunológicos. De igual forma discuten los aspectos terapéuticos, complicaciones y los criterios actuales de cura de esta condición. Es la opinión de la Junta Editora que este resumen debe ser de gran interés y ayuda práctica para todos nuestros lectores.

- \* **Human Small Bowel Preservation: Assessment of Viability During Storage** ..... 336  
*Luis H. Toledo Pereyra, MD, PhD and John S. Najarian, MD*

En este artículo Toledo-Pereyra y Najarian presentan los resultados de experimentos hechos en intestinos delgados obtenidos de cadáveres humanos y preservados por 24 horas por cuatro técnicas diferentes. Después de 24 horas de preservación los intestinos fueron trasplantados a la fosa ilíaca de perros. Después de trasplantados los intestinos fueron evaluados para cambios vasculares, alteraciones macroscópicas, sangría y cambios en la mucosa y serosa.

Los autores reportan que los intestinos preservados con perfusión pulsátil a temperaturas bajas demuestran mejor viabilidad funcional que aquellos preservados a temperaturas bajas sin perfusión pulsátil.

Los autores revisan la literatura y resumen los problemas técnicos e inmunológicos que caracterizan el trasplante de intestino delgado. Entre estos se encuentra la gran cantidad de tejido linfático en el intestino delgado. Esto hace que la respuesta inmunológica sea mucho más intensa al compararse con el trasplante de otros órganos.

Aunque este artículo es altamente técnico, la discusión es práctica e informativa.

- \* **The Use of Frozen Semen for Artificial Insemination** ..... 342  
*Walter M. Pinedo, MD, FACOG and Rafael A. Rodríguez Acevedo, MD*

In this communication the authors present their experience with 3 patients referred for artificial insemination to the Mayaguez Medical Center. Pinedo and Rodríguez Acevedo thoroughly discuss the procedure, alternatives to the procedure, complication and success rates.

A complete fertility work up should be performed on the patient. This should include T<sub>3</sub>, T<sub>4</sub> plasma progesterone and if needed endometrial biopsy. Cervical, uterine or tubal abnormalities should be carefully discarded.

At a time when adoption patterns and adoption laws have dramatically changed, this procedure presents an adequate alternative for the appropriate candidate.

- \* **Editorial: Educación Médica en Puerto Rico** ..... 347  
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## UPDATE ON SARCOIDOSIS

D. Geraint James, MA, FRCP, MD and R. E. Figueroa Lebrón, MD, FCCP

(1)

(2)

**Resumen:** Luego de finalizada la Octava Conferencia Internacional sobre la Sarcoidosis hemos querido ofrecer a los lectores los conceptos nuevos, las hipótesis más o menos favorecidas para proveerles de un esquema moderno a la luz de las investigaciones más recientes de la fascinante enfermedad que es la Sarcoidosis y que por ser común en Puerto Rico es de sumo interés para todos los médicos de Puerto Rico.

### Introduction

The Eighth International Conference on Sarcoidosis was held in September 1978 in Cardiff with 300 participants from 32 countries. The transactions of this conference will be published within the next six months providing new views and information on this enigma which continues to fascinate, delight and infuriate clinicians, immunologists and epidemiologists alike. This review condenses these expert opinions until the transactions become available.

Sarcoidosis is but one member of a large family of granulomatous disorders, which include infections, chemicals, neoplasia, enzyme defect, extrinsic allergens or immunological deficiency (Table I). The common thread is

the epithelioid cell sarcoid granuloma, which is metabolically active and secreting a wide range of interesting enzymes (Fig. 1).

### Description of Sarcoidosis

Sarcoidosis is a multisystem granulomatous disorder of unknown aetiology most commonly affecting young adults and presenting most frequently with bilateral hilar lymphadenopathy, pulmonary infiltration, skin or eye lesions. The diagnosis is established most securely when clinicoradiographic findings are supported by histological evidence of widespread non-caseating epithelioid cell granulomas in more than one organ or a positive Kveim-Siltzbach skin test. Immunological features are depression of delayed-type hypersensitivity suggesting impaired cell-mediated immunity and raised or abnormal serum immunoglobulins suggesting lymphoproliferation. There may also be hypercalciuria with or without hypercalcaemia. The course and prognosis correlate with the mode of onset; and acute onset with erythema nodosum usually heralds a self-limiting course and spontaneous resolution while an insidious onset may be followed by relentless progressive fibrosis. Corticosteroids relieve symptoms and suppress inflammation and granuloma formation.

### Epidemiology

Sarcoidosis is tenfold more frequent in

---

(1) From the Royal Northern Hospital, London N.7 and (2) the Regent American College of Chest Physicians.

Reprints to: Ramón E. Figueroa, MD, Suite 607, 400 Domenech Ave., Hato Rey, Puerto Rico 00919.

TABLE I

## A Classification of Granulomatous Disorders

---

<b>Infections</b>	<b>Chemicals</b>
<i>Fungi</i>	<i>Beryllium</i>
<i>Histoplasma</i>	<i>Zirconium</i>
<i>Coccidioides</i>	<i>Silica</i>
<i>Blastomyces</i>	<i>Starch</i>
<i>Sporotrichum</i>	<b>Immunologic Deficiency</b>
<i>Protoza</i>	<i>Sarcoidosis</i>
<i>Metazoa</i>	<i>Crohn's Disease</i>
<i>Toxoplasma</i>	<i>Primary biliary cirrhosis</i>
<i>Leishmania</i>	<i>Weener's granulomatosis</i>
<i>Toxacara</i>	<i>Giant cell arteritis</i>
<i>Schistosoma</i>	<i>Peyronie's disease</i>
<i>Spirochaeta</i>	<i>Hypogammaglobulinemia</i>
<i>T pallidum</i>	<i>Systemic lupus erythematosus</i>
<i>T pertenuis</i>	<b>Leukocyte Defect</b>
<i>T carateum</i>	<i>Chronica granulomatous disease of childhood</i>
<i>Mycobacteria</i>	<b>Extrinsic Allergic Alevolitis</b>
<i>M tuberculosis</i>	<i>Farmer's lung</i>
<i>M leprae</i>	<i>Bird Fancier's</i>
<i>Anonymous</i>	<i>Mushroom worker's</i>
<i>BCG</i>	<i>Suberosis (cork dust)</i>
<i>Bacteria</i>	<i>Bagassosis</i>
<i>Brucella</i>	<i>Maple bark stripper's</i>
<b>Other infections</b>	<i>Paprika splitter's</i>
<i>Car scratch</i>	<i>Coffee bean</i>
<i>Lymphogranuloma</i>	<b>Other</b>
<i>Neoplasia</i>	<i>Pyrexia of unknown origin</i>
<i>Carcinoma</i>	<i>Radiotherapy</i>
<i>Reticulosis</i>	<i>Cancer chemotherapy</i>
<i>Pinealoma</i>	<i>Panniculitis</i>
<i>Dysgerminoma</i>	<i>Chalazion</i>
<i>Seminoma</i>	<i>Sebaceous cyst</i>
<i>Reticulum cell sarcoma</i>	<i>Dermoid</i>
<i>Malignant nasal granuloma</i>	<i>Hepatic granulomatous disease</i>
	<i>Sea urchin spine injury</i>

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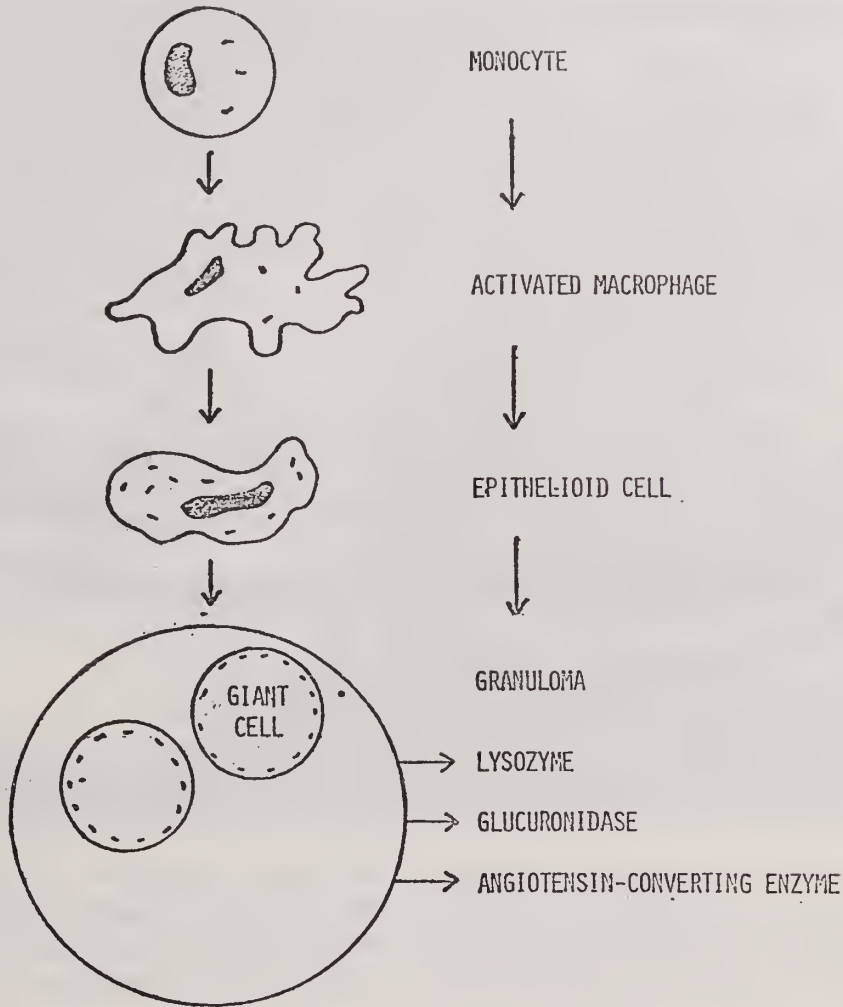


Figure 1: A sarcoid granuloma is the battlefield between indigestible antigen and activated macrophages. It secretes several interesting enzymes.

the American negro than in the white population and a sarcoidosis profile is also different in the two groups. One third of the black sarcoidosis patients, compared with only 2 percent of the whites, were born in the south eastern states. Female preponderance was only noted in the black patients. Respiratory symptoms, pulmonary infiltration, fever, weight loss, skin and eye lesions are significantly more common in blacks. Serum globulin elevations

and eosinophilia are largely confined to blacks.

The previously held view that sarcoidosis is rare in the black population of South Africa is no longer tenable. A recent survey at Groote Hospital, Cape Town, reveals an incidence per 100,000 of 17 in coloured, 27 in black and six in white patients. Only in black patients were skin lesions widespread or florid. This accounts for the mistaken diagnosis of leprosy in the past.



Figure 2: Sarcoidosis is an iceberg syndrome. New investigative techniques are uncovering latent forms of the disease.

Sarcoidosis is commonly seen in West Indians in London and in Martinique in Paris. It is now being systematically sought and found in Jamaica where it predominates in male negro or mixed-blood patients presenting with respiratory symptoms, pulmonary infiltration and weight loss. More than 70 percent are tuberculin negative. The majority are from urban areas and the lower socio-economic groups.

In Puerto Rico the disease is widely present affecting females with a slight preference over men of about 4 to 3. Most of our patients are below 40 years of age and the onset is acute in presentation; so much so, that erythema nodosum in a young puertorrican of either sex should suggest to the physician the great possibility of sarcoidosis.

### An Iceberg Syndrome

Sarcoidosis is an iceberg syndrome for ma-

ny forms of the disease lie undetected (Fig. 2). We must dig deeper to uncover latent forms of the disease. As new techniques emerge, they help to detect excitingly new clinical manifestations of the disease. When fluorescein angiography was introduced, it revealed leaking retinal veins which were promptly sealed by corticosteroid therapy (Fig. 3). Likewise, brain-scans brought a new dimension visualising space-occupying sarcoid granulomas and ventricular block due to them (Fig. 4).

Sarcoidosis of the heart is another example for it is difficult to recognize clinically and may only be revealed for the first time at autopsy. It should be suspected if a patient with a multisystem disorder develops heart block, bundle branch block, arrhythmias, congestive cardiac failure, pericarditis or cardiomyopathy. No portion of the heart is immune to infiltration by sarcoid granulomas but the myocardium is by far the most frequently involved, particularly



Figure 3: Fluorescein angiography reveals leaking retinal vein involvement by sarcoidosis, with considerable improvement following steroid therapy. (By kind courtesy of Mr. Michael Sanders.)

the ventricular free wall, followed by the ventriculum septum, the right ventricle, and, lastly, the atrial wall. Involvement of the pericardium and endocardium should be regarded as but an extension of the myocardial granulomatous process (Fig. 5).

### Pathology

The epithelioid cell granuloma in sarcoidosis comprises macrophages, fibroblasts, activated lymphocytes, giant cells and epithelioid cells. This conglomeration is evenly dis-

tributed and largely replaces the T zones of the lymph node. The interdigitating reticulum cells of the T zones are unaffected by granuloma formation and can be demonstrated within granulomas. Epithelioid and giant cell granulomas are characterized by numerous mitochondria, electron dense vesicles (lysosomes) and interdigitating processes. There is a close relationship between granuloma formation and blood vessels, as in diabetic microangiopathy. In the central nervous system, this is particularly evident in the walls of veins and capillaries, producing granulomatous periphlebitis. This is shown most elegantly by venous leakage





Figure 4: Brain scan discloses ventricular block due to sarcoid deposits.

with fluorescein angiography in retinal sarcoidosis. Pulmonary artery involvement is also noted in the media and adventitia of large and small pulmonary arteries.

Asteroid bodies are composed of microfilaments and microtubules, intertwining within a star. They contain lipid residual bodies, which may be responsible for the development of Schaumann bodies.

Ion microprobe mass analysis is very sensitive for very light elements such as beryllium and for very low concentrations (less than one part per million) of many elements. This technique has disclosed beryllium, zirconium, aluminium and tungsten in granulomatous disorders other than sarcoidosis. This highly sensitive probe is now underway for possible sarcoidosis antigens.

### Diagnosis

#### Histology

When confronted with a compatible

clinical picture, seek histological confirmation as soon as possible by means of skin or lymph node biopsy, fiber-optic bronchoscopy, aspiration liver biopsy or Kveim-Siltzbach skin test.

#### *Serum angiotensin-converting enzyme (SACE)*

The epithelioid-cell sarcoid granuloma secretes several enzymes, some of which can be measured in the serum. SACE is raised in about 50 percent of patients with active sarcoidosis. It falls to normal with steroid therapy and then rises again when steroids are discontinued and active sarcoidosis persists or recurs. It may, therefore, be helpful in following the course of the disease, and particularly in heralding a relapse. False-positive elevations are extremely infrequent in respiratory disorders that mimic pulmonary sarcoidosis, but they have been observed in Hodgkin's disease, leprosy, primary biliary cirrhosis and Gaucher's disease.

#### *Poor T cell function*

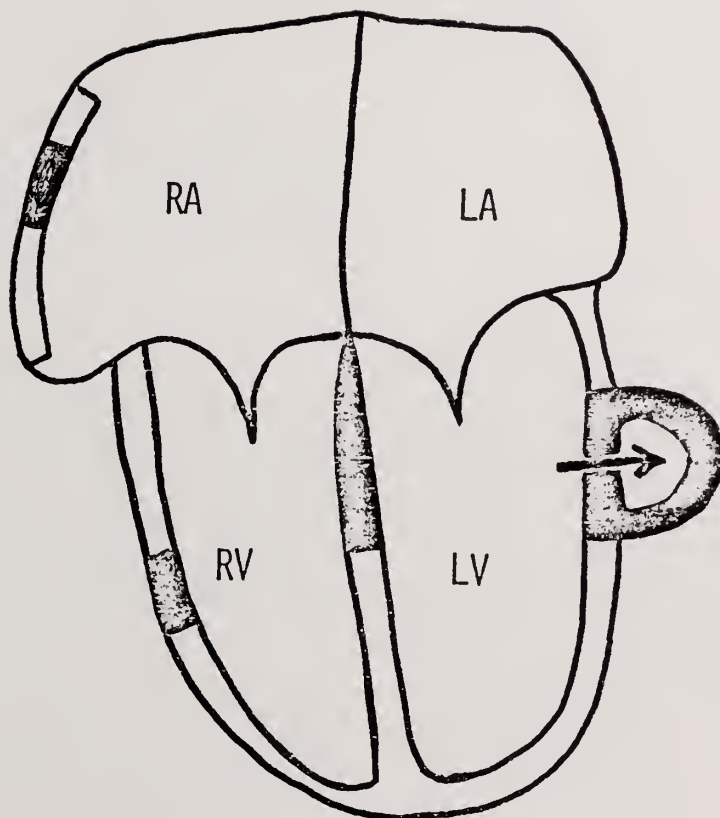


Figure 5: Sites of cardiac sarcoid granulomas. The arrow defines possible aneurysmal dilatation of the wall of the left ventricle.

This is evident by depression of delayed-type hypersensitivity using such recall skin antigens as tuberculin and dinitrochlorobenzene.

#### *Exhuberant B cell overactivity*

This is reflected by elevated or abnormal serum immunoglobulins, and increased serum antibodies of Epstein-Barr virus, herpes, rubella and chlamydia.

#### *Calcium metabolism*

Hypercalcemia and hypercalciuria are such well-recognized markers that they have been

incorporated into the descriptive definition of sarcoidosis. Hypercalciuria is more frequent than hypercalcaemia, so a normal serum calcium level does not exclude abnormal calcium metabolism. Twenty-four hour urine calcium levels should be done routinely.

#### *Treatment*

Corticosteroids remain the sheet-anchor of treatment, being used by mouth and by topical application.

#### *Route of administration*

Topical steroids are administered for irido-

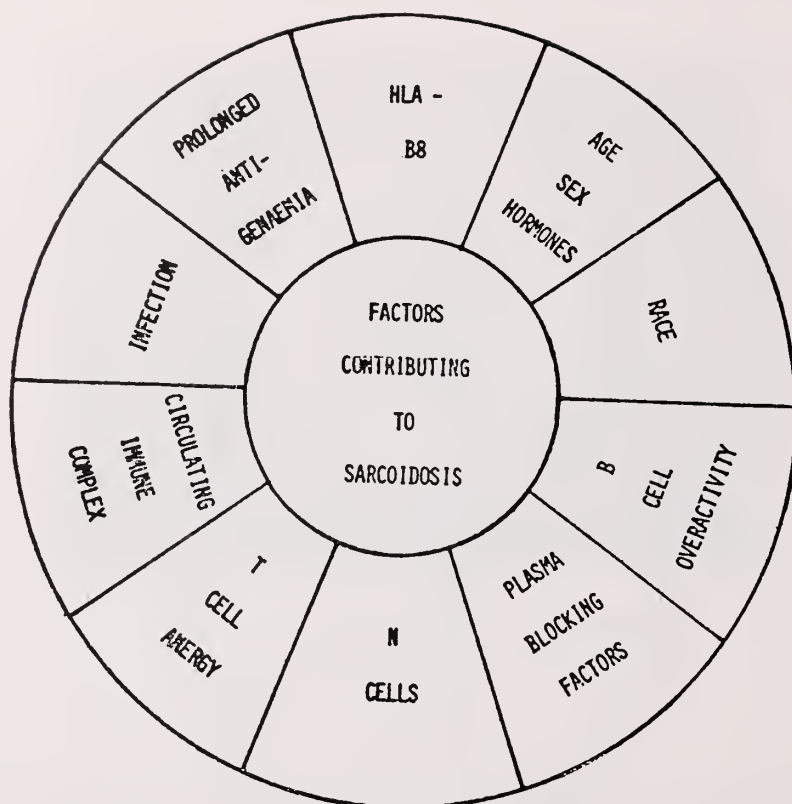


Figure 6: Background contributory factors predisposing to sarcoidosis.

cyclitis in the form of eye drops during the day, reinforced with a corticosteroid eye ointment at night. If there is no substantial and continuing improvement during ten days, then the concentration of corticosteroid in the anterior segment of the eye may be increased by a local subconjunctival depot of cortisone. Oral corticosteroids are indicated if local treatment does not lead to a rapid response or if there is evidence of posterior uveitis. Likewise triamcinolone acetonide (Lederle) may be injected directly into disfiguring skin plaques with great benefit, alone or in conjunction with oral steroids.

#### *Indications for steroid therapy*

They include ocular involvement, pul-

monary infiltration, breathlessness, persistent hypercalciuria, disfiguring skin lesions, neurological disease, myocardial involvement, hypersplenism, and enlargement of lacrimal and salivary glands.

#### **Other Drugs**

*Oxyphenbutazone* is of value in acute exudative sarcoidosis but not in the chronic fibrotic form of the disease. Like steroids, it controls symptoms but also suppresses the development of sarcoid tissue and it may suppress the evolution of the Kveim nodule.

*Indomethacin*. This is also effective in the acute exudative stage, particularly acute sarcoid uveitis. It should be considered as an alter-



native to steroids if they are contraindicated because of diabetes, hypertension or osteoporosis.

*Chloroquine.* It has no value in the acute disease but it is helpful in the management of lupus pernio and pulmonary fibrosis as an antifibrotic agent. It should be given in doses of 200 mg on alternate days for periods of no longer than nine months.

*Potaba.* Potassium para-aminobenzoate is also helpful because of its antifibrotic effect. Three-gram envules are taken by mouth four times daily for several months. It provides an effective alternative to corticosteroids and chloroquine, and giving all three in rotation helps to overcome the undesirable longterm complications of steroids and chloroquine.

*Methotrexate.* It is most valuable in the treatment of troublesome skin plaques and lupus pernio. Because of its hepatotoxicity, it is limited to weekly oral doses of 25 mg. Improvement may be expected within four months, but relapses may also be anticipated within a month of discontinuing treatment.

*Azathioprine* can be used with advantage in combination with longterm steroids, allowing the dose of the latter to be halved and thereby minimizing the adverse longterm effects of steroids. This steroid-sparing effect of azathioprine is particularly welcome in the diabetic, the hypertensive and in older osteoporotic patients.

### Persistent hypercalciuria

Hypercalciuria is swiftly controlled by oral steroids. If they are contraindicated, then there are alternative means of preventing overabsorption of calcium. There is an effective and palatable effervescent phosphate

preparation (Sandoz) containing 500 mg elemental phosphate. Sodium cellulose phosphate is also effective in a dose of 5 grams three times daily with food.

### Criteria of Cure

How do we define whether sarcoidosis is cured, arrested or quiescent? The patient and doctor want to know the answer to this riddle and so do employers, insurance companies and others involved in the malady. Criteria of cure are constantly changing from the old days of resolution of skin lesions, clearing of chest radiographic abnormalities, restoration of normal T cell function with a positive tuberculin skin test reaction, a negative Kveim test, disappearance of hypercalcaemia and hypercalciuria, and a fall of a raised serum angiotensin-converting enzyme to normal levels (Table II).

### Etiology

The cause of sarcoidosis remains unknown. We do not know whether it is one disease or whether there are many contributing factors (Fig. 6).

### Infection

Many organisms provoke a non-specific granulomatous reaction but this should not be misconstrued as multisystem sarcoidosis. Helminths provoke such reactions in the liver and CNS, anonymous mycobacteria cause swimming pool and fish-tank granulomas and *Mycobacterium leprae* produces confusingly similar granulomas. Sarcoidosis was once thought to be caused by the human tubercle bacillus

TABLE II

Criteria of cure of Sarcoidosis during the last Century

---

YEAR	CRITERIA OF CURE
1878	<i>SKIN LESION SUBSIDES</i>
1914	<i>CHEST RADIOGRAPH CLEARS</i>
1935	<i>SERUM PROTEINS FALL</i>
1941	<i>KVEIM TEST NEGATIVE</i>
1958	<i>NORMAL CALCIUM METABOLISM</i>
19 SIXTIES	<i>T CELLS WAKE UP</i> <i>TUBERCULIN NEGATIVE TO POSITIVE</i> <i>PHYTOHAEMAGGLUTININ TRANSFORMA-</i> <i>TION</i>
19 SEVENTIES	<i>SERUM ANGIOTENSIN-CONVERTING</i> <i>ENZYME (SACE) FALLS</i>

---

but there are many important points differentiating sarcoidosis from tuberculosis. Fungi and protozoa have also been incriminated.

Claims for a causal virus are longstanding, and at various times, mumps, influenza, parainfluenza, Newcastle agent and measles virus particles have been isolated. High titers of antibodies to several viruses have been noted, but this is more likely to reflect lymphoproliferation by exuberant B cells than a viral etiology of the disease.

The occasional occurrence of familial sarcoidosis suggests possible genetic influences. The evidence suggests a racial predisposition to familial sarcoidosis and a recessive mode of inheritance for susceptibility. Our HLA antigen studies also indicate that there is an inherited susceptibility to arthritis and erythema nodosum with B8 as a genetic marker.

#### Allergy

Genetic and Racial Factors

Inhalation of pine pollen and peanut

dust, clay-eating and chewing pine pitch have all been incriminated as contributory regional factors in different areas.

### Chemical

Beryllium and zirconium are known to produce sarcoid granulomas in the sensitized individual, but other elements do not seem to have this effect. Exhaustive skin testing with metals and other inorganic elements in sarcoidosis patients and controls has not revealed any peculiar hypersensitivity to chemicals. Skin tests for sarcoidosis, beryllium and zirconium disease and leprosy are very similar in that a sarcoid granuloma is found in the injection site one month after inoculation. Each skin test is individually specific for its own disorder and there is no overlap.

### Autoimmune Disorder

There are certain well recognized indicators of an autoimmune disorder and sarcoidosis does not fulfill all these criteria satisfactorily. There is one pattern of sarcoidosis that could conceivably fit, namely erythema nodosum with hilar adenopathy, a syndrome which may be associated with a circulating immune complex; and these immune complexes have been shown to be present in sarcoidosis.

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Recent advances in our knowledge of

sarcoidosis are based on the numerous international contributions to the Eighth International Conference on Sarcoidosis and other Granulomatous Disorders, Cardiff, September 1978. It is anticipated that the transactions will be available by March 1979. They will be published by Alpha Omega Publishing Limited, Cardiff.

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**INDICATIONS:** For the prevention and treatment of nocturnal recumbency leg muscle cramps, including those associated with arthritis, diabetes, varicose veins, thrombophlebitis, arteriosclerosis, and static foot deformities.

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### DOSAGE AND ADMINISTRATION:

1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

Product Information as of September, 1977

U.S. Patent 2,985,558

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**Contraindications and Cautions:** There are no known contraindications to oral use when administered in recommended doses. Should not be given immediately postpartum or in the presence of arterial bleeding.

Parenteral administration is not recommended in the presence of hypotension or tachycardia.

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U.S. Pat. No. 3,056,836

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## HUMAN SMALL BOWEL PRESERVATION: ASSESSMENT OF VIABILITY DURING STORAGE

Luis H. Toledo-Pereyra, MD, PhD and John S. Najarian, MD

**Resumen:** La viabilidad del intestino humano fue estudiada durante perfusión pulsátil o almacenamiento a bajas temperaturas por diferentes períodos de tiempo. Ocho intestinos humanos fueron preservados en 1) perfusión pulsátil a bajas temperaturas con plasma crioprecipitado o plasmanate, 2) almacenamiento a bajas temperaturas en solución de Collins (C-3) (4°C) o 3) una combinación de almacenamiento y perfusión a temperaturas bajas. Los intestinos humanos preservados en perfusión pulsátil a bajas temperaturas tuvieron una mejor viabilidad que los intestinos almacenados únicamente a temperaturas bajas sin perfusión.

**Summary:** The viability of human small bowels was assessed during hypothermic pulsatile perfusion or storage for variable periods of time. Eight bowels were preserved by (1) hypothermic pulsatile perfusion with human cryoprecipitated plasma or plasmanate; (2) hypothermic storage in Collins solution (C-3) (4°C), or (3) hypothermic storage (6 hr.) followed by perfusion with plasmanate (18 hr.). The small

bowels preserved by hypothermic pulsatile perfusion had better functional viability results during perfusion than those stored hypothermically.

Clinical attempts to transplant the human small bowel have had such discouraging results that no consistent research to preserve the organ for further human trials has been recently undertaken. The small bowel has unique physiological and immunological characteristics, particularly when compared to other transplantable organs such as the kidney, heart and liver. For example, the quantity of lymphatic tissue in the intestine itself, and in its mesentery, contribute to the rapid rejection phenomenon that frequently occurs in the transplanted small bowel. In addition, the initial decrease in the small bowel's absorptive ability, combined with the complete denervation and interruption of the lymphatics during grafting, further contribute to its poor postoperative function.

In 1972 Ruiz and Lillehei (1) reviewed the five reported cases of clinical intestinal allotransplantation. There were no long-term survivors. The post-transplant complications that lead to death were related to hyperacute rejection, small bowel necrosis, progressive graft rejection, gastrointestinal bleeding, and profound metabolic alterations.

We have previously shown that the canine small bowel can be preserved by hypothermic pulsatile perfusion up to 24 hours,(3, 7). When transplanted, these bowels show minimal signs

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of damage and the dog recipients survive for long periods of time with only moderate doses of immunosuppressive drugs (7). Encouraged by these laboratory results, we decided to evaluate the characteristics of the human small bowel after 24 hours of pulsatile perfusion or hypothermia, alone, and after xenografting into mongrel dogs.

## Materials and Methods

### *Small Bowel Preservation Methods*

The small bowels from eight human cadavers (14-47 years old) were preserved for 24 hours by one of four methods. Method I (2 bowels), hypothermic pulsatile perfusion with human cryoprecipitated plasma; Method II (3 bowels), hypothermic pulsatile perfusion with human plasmanate; Method III (1 bowel), preservation by hypothermia in Collins solution (C-3); and Method IV (2 bowels), hypothermic storage in Collins solution (C-3) (6 hours) followed by perfusion with plasmanate (18 hours). The functional assessment of each bowel was evaluated during preservation and after xenotransplantation into a mongrel dog.

### *Operative Technique*

The small bowels of cadaver donors were obtained after routine bilateral donor nephrectomy had been completed for kidney preservation for transplantation. The small bowels were dissected at their main vascular structures; the superior mesenteric artery and the superior mesenteric vein. The distal portion of the small bowel was resected one inch from the ileocecal valve, and the proximal portion was resected at the level of the second portion of the duodenum after the duodenum was detached from the ligament of Treitz. After the vessels were clamped and divided, the organ was removed and placed in 4°C saline solution. The superior mesenteric artery was cannulated and flushed with Ringer's lactate at 4°C containing 0.1 gm/L of procaine and 10,000 U/L of heparin until the venous effluent was clear. Five small bowels were preserved by pulsatile perfusion, one small bowel was

preserved under hypothermia alone; and two small bowels were preserved by both methods.

After 24 hours of preservation, each small intestine was xenotransplanted into the iliac fossa of a mongrel dog. The iliac vessels of the recipient were used for vascular anastomosis with the mesenteric vessels of the donor. The small bowels were assessed for vascular changes, macroscopic alterations, bleeding, and changes in the mucosa and serosa. A biopsy for light histology was taken immediately after transplantation and every 10 minutes until macroscopic organ rejection was obvious.

### *Perfusion and Preservation Techniques*

The perfusion system (7°C temperature, pH 7.4, oxygen pressure 200 mm Hg, pulse rate 60/min., and systolic pressure 60 mm Hg) (7) was primed with 1,000 ml of either human cryoprecipitated plasma, or a commercial human plasmanate (Cutter Laboratories, Inc., Berkeley, CA.). The human frozen plasma was double thawed and filtered and, 1gm/L of magnesium sulfate, 80 U/L of regular insulin, 2ml/L of phenosulfonthalein, 500mg/L of kanamycin, 1gm/L of ampicillin, and 500 mg/l of methylprednisolone were added to the plasma (7). Flow rate, perfusion pressure, fluid loss, weight gain, lactate dehydrogenase (LDH) and glutamic oxaloacetic transaminase (GOT) in the perfusate were noted initially and then at 2, 6, 12, and 24 hours. D-xylose (10 gm in 100 ml of water) was infused into the cannulated portion of the duodenum immediately after perfusion began and again at 12 hours (7). Samples of the perfusate were taken at 30 minute intervals for 4 hours. Intraluminal small bowels excretion samples for the determination of proteins and electrolyte levels were collected every 6 hours. The small bowel which received only hypothermic storage was transferred to the perfusion system at 12 hours to obtain perfusion determinations for one hour only. The fluid loss that occurred during perfusion was equivalent in our system to the amount of fluid added at any time after the perfusion was begun.

### *Statistical Analysis*

The results from the preservation studies were analyzed by the chi-square test. Mean  $\pm$  the standard

TABLE I  
Characteristics of Small Bowel Cadaver Donors, Before and During Bowel Excision

		TREATMENT		Length of Warm Ischemia(Minutes)
		Before Excision	During Excision	
Group I	1. None		Heparin, mannitol, *ALG, furosemide	18
	2. none		Heparin, furosemide, ALG, methylprednisolone	22
Group II	1. none		Heparin, furosemide, ALG	60
	2. furosemide, adrenalin, methylprednisolone		Heparin, mannitol, ALG	35
	3. none		Heparin, furosemide, methylprednisolone	30
Group III	1. mannitol, metaraminol		Heparin, mannitol, ALG, furosemide	10
Group IV	1. furosemide, mannitol isopreterenol		Heparin, mannitol, ALG furosemide	30
	2. none		Heparin, furosemide, ALG	27

\* – Antilymphocyte globulin

error (SE) of the mean was determined in all preservation samples. All small bowels were included in the results.

Results

Table I illustrates the characteristics of the cadaver donors before and during excision

of the small bowels. Variable amounts of heparin, mannitol, furosemide, and either methylprednisolone or antilymphocyte globulin (ALG), or both, were given intravenously to all donors during the excision procedure.

*Hypothermic Pulsatile Perfusion with Cryoprecipitated Plasma (CPP)*



The perfusate flow of these two bowels was good and their effluents ran clear after the initial flushing with 800 ml of Ringer's lactate. Edema of the mesentery was obvious during the second and third hour of perfusion but did not increase thereafter. There was moderate edema of the loops at the end of perfusion. After 18 hours of preservation, there were moderate increases in the systolic perfusate pressure (68 mm Hg). The flow was kept constant at 0.5-0.4 ml/min/gm., and the average pH was 7.6. After 24 hours of perfusion, there was a 20-40 percent average increase in bowel weight and a moderate increase of the cytoplasmic enzymes (LDH 160/UL, GOT 60 U/L). There were no significant changes in the electrolytes and osmolarity at any time. During the first hour of perfusion, 300-400 ml of perfusate fluid was lost. The bowel loops were dilated, and in the next two hours, another 1200 ml of fluid was lost. At the end of 24 hours of preservation, the total loss of fluid was equivalent to 2.5 liters. The D-xylose response at 24 hours (120 min after infusion) was 3.0 mg percent.

Immediately after the xenotransplantation and the vascular clamps were removed, the bowels returned to their normal pink color, and bowel secretions were observed. The loops showed minimal signs of edema and no hemorrhagic necrosis or bleeding were noted. Xenograft rejection began within 10-15 minutes after transplantation. The histologic examination that followed, revealed lymphocyte infiltration, and moderate villi destruction.

#### *Hypothermic Pulsatile Perfusion with Plasmanate*

There were no significant differences in flow rate and perfusion pressure between these 3 bowels and the 2 bowels perfused with CPP. The flow remained constant at 0.5 ml/min/gm until the end of preservation. The systolic

perfusion pressure remained constant at 60 mm Hg. During the first hour of perfusion, 500 ml of fluid were lost, and at the end of 24 hours, a total of 2 liters had been lost. These bowels gained an average of 30 percent weight during the whole perfusion period. The intracytoplasmic enzymes at 24 hours showed: LDH 140 U/L and GOT 80 U/L. The sodium, potassium, and osmolarity levels remained unchanged. The D-xylose response at 24 hours (120 min after infusion) was 3.5 mg percent.

Immediately after xenografting, the mucosa and serosa were moderately inflamed, and the mesentery was edematous. Although there were no signs of motility, there appeared to be no definite areas of necrosis or bowel damage. The xenograft rejection reaction occurred within 20 minutes after revascularization.

#### *Hypothermic Storage in Collins Solution (C-3)*

One liter of fluid was lost by this small bowel during its first 12 hours of hypothermic storage. The fatty tissue around the mesentery and loops were hard and edematous when the bowel was first placed in the preservation machine. After 12 hours of preservation, there was evident damage to the mucosa and serosa, and the mesentery. The flow was decreased (0.25 ml/min/gm) and the systolic pressure increased (72 mm Hg). At 12 hours of storage, the bowel had gained an average of 20 percent of its original weight, the loops were edematous, and the mesentery was inflamed. At 12 hours after preservation, the LDH (200 U/L) and GOT (100 U/L) were increased and the D-xylose (120 min, sample) was 2 mg/100 ml. Ten minutes after xenografting, the mucosa and serosa darkened, the mesentery became inflamed, there were no signs of motility, and there were obvious spots of mesenteric hemorrhage. The bowel loops were significantly distended and there were signs of hemorrhagic necrosis. The microscopic examination showed severe damage

to the mucosa and villi.

### *Hypothermic Storage Followed by Plasmanate Perfusion*

The perfusion characteristics of these two bowels were similar to the other perfused bowels. After 12 hours of pulsatile perfusion the fluid loss reached 2.0 L and there was no need for additional perfusate. The pulsatile flow was low (0.3 ml/min/gm) during hypothermic storage, but was kept at 0.5 ml/min/gm during the perfusion period. There were no significant pressure changes. The enzyme levels were within normal limits at the middle of the perfusion period. The D-xylose (120 min. sample) levels reached approximately 3 mg/100 ml during the first 12 hours of perfusion and remained stable until the end of the study. Immediately after xenografting the mucosa and serosa of the bowel became slightly dark in hue. The mesentery was inflamed and there were areas of minimal mesenteric hemorrhage. Xenograft rejection occurred within 25-30 minutes after transplantation. Histologic examination revealed characteristics similar to those observed on the perfused bowels.

### Discussion

Small bowels preserved by hypothermic pulsatile perfusion had better functional viability potential than small bowels subjected to hypothermic storage alone. The bowels perfused with either CPP or plasmanate combined with hypothermic perfusion had minimal signs of damage after 24 hours of perfusion. In addition, xenograft rejection of these two groups of perfused bowels were delayed, compared to the rejection phenomenon of the bowels preserved by storage.

The small bowel has several distinct characteristics which complicate its use for

clinical transplantation (1). First, the large amount of lymphatic tissue in the small bowel probably makes its immunological response more intense than that of other transplantable tissues. Conceivably, the small bowel could enlist a hyperacute rejection, or graft vs. host reaction, when transplanted between human beings. Therefore, an adequate immunosuppressive regimen unique to the small bowel must be available before further human trial are begun. Secondly, because severe impairment of the small bowel's absorption function takes place during the first 3-4 weeks of transplantation (5, 6), hyperalimentation must be used to keep the recipient alive until the bowel's natural functions resume. Third, there is no adequate means to assess the immunological or functional viability of the organ after transplantation; the only values available are the histological specimens, or carbohydrate and fatty acids absorption curves (6). Fourth, large spectrum antibiotics may reduce the possibility of endotoxemia in unprepared bowels prior to, or during preservation (4).

Compounding the functional impairment of the transplanted small bowel are the problems involved with the non-sterile donor organs available for preservation. Previous experiments in dogs suggest that donor bowels

that have not received antibiotic treatment before excision or during preservation, have a higher incidence of endotoxemia than bowels that have antibiotic treatment (4). Therefore, intensive antibiotic treatment of the small bowel should be instituted during preservation.

We did not obtain complete functional or immunological studies of the xenograft reaction. Our results only suggest that the two human small bowels preserved by hypothermia for the first 6 hrs. and then by human plasmanate for the remaining 18 hours had delayed xenograft rejection. The first signs of rejection appeared

within 25-30 minutes after xenografting. Even though delayed, endothelial destruction, intravascular congestion, and interstitial mononuclear infiltration occurred. Rejection of organ grafts between widely divergent species is apparently caused by the reaction of preformed recipient antibodies with the graft endothelium (2). Improved immunosuppressive techniques may prolong or suppress the immune response in organs with a high antigenic potential.

The small bowel that was preserved by hypothermic storage for 24 hours showed poor functional signs prior xenografting. On the other hand, bowels that were preserved by hypothermic pulsatile perfusion functioned adequately before xenograft rejection. The bowels preserved by the methods of hypothermic storage and perfusion showed no significant functional repairment until rejection began. Hypothermia, oxygenation, stable pH levels, plasma perfusates, and pulsatile perfusion are important factors in the preserva-

tion of the small bowel.

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# THE USE OF FROZEN SEMEN FOR ARTIFICIAL INSEMINATION

Walter M. Pinedo, MD, FACOG and Rafael A. Rodríguez Acevedo, MD

**Summary:** There is a growing appreciation that clinical use of frozen human semen is a practical, fairly successful, safe and valuable method of artificial insemination as is evidenced by the large series of several authors (5-6). Great efficiency is secured in the matching of relevant genetic and gross phenotypical characteristics of donor, husband, and recipient by using frozen-preserved donor semen.

Donor insemination with frozen semen results in about a 50 percent success rate. The ready availability of semen and the use of the same donor on repeated occasions for a particular woman are major advantages. Disadvantages include ultrastructural changes in the acrosome area of spermatozoa and a 50 percent reduction in the original motility of spermatozoa frozen and subsequently thawed.

Our first patient became pregnant in 1976; her husband had had a previous vasectomy and two plastic operations for recanalization of vas deferens were unsuccessful. She delivered a baby girl by cesarean section that weighed 8 lbs. 5 oz. The second patient, whose husband is a case of Klinefelter's syndrome became pregnant after AI was done twice. She delivered twin baby girls. The third patient, whose husband was also a case of Klinefelter's

syndrome (azoospermia) was unsuccessful after two AI.

**Resumen:** Existe una creciente aceptación de que el uso clínico de semen congelado es un método práctico, más o menos de un éxito seguro y valioso como lo evidencian los cuantiosos informes presentados por diferentes autores hasta el presente.

Tres casos fueron presentados. Nuestra primera paciente quedó embarazada en el 1976. Dos previas operaciones practicadas a su esposo para tratar de recanalizar el conducto deferente no fueron exitosas. Ella tuvo una niña por operación cesárea en 1977 que pesó 8 libras, 5 onzas después de su primera inseminación con semen congelado de un donante.

A la segunda paciente, cuyo esposo era un caso de síndrome de Klinefelter, se le hizo inseminación artificial dos veces y en la última quedó embarazada. Tuvo gemelas a las 35 semanas de gestación.

A la tercera paciente, cuyo esposo también es un caso de síndrome de Klinefelter, se le efectuó la inseminación artificial dos veces sin resultado alguno.

Irreversible male infertility is often a difficult psychological problem for the infertile couple. The only alternative for a chronically deficient male is artificial insemination of the female with donor's semen. However, the husband's ego is often threatened and there

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TABLE I

Diagnostic Studies Performed in the Female Prior to Artificial Insemination

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MINIMAL DIAGNOSTIC PROCEDURES

1. *History and physical examination*
  2. *Laboratory studies*
    - a. *Blood count and sedimentation rate*
    - b. *Serology*
    - c. *Urinalysis*
    - d. *VDRL*
    - e. *Type and RH*
    - f. *T3 and T4*
    - g. *Progesterone in blood*
  3. *Postcoital test*
  4. *Endometrial biopsy*
  5. *Tubal insufflation and/or hysterosalpingogram*
  6. *Miscellaneous*
    - a. *Papanicolaou's stain*
    - b. *Fern test-spinnbarkeit*
    - c. *Serial vaginal cytology*
    - d. *Hangingdrop for Candida and Trichomonas*
    - e. *Incompatibility test - cervical mucus and semen.*
- 

may be questions in the couple's minds regarding the legitimacy of children born following artificial insemination (1).

Because of these real or imagined problems presented by AI, many couples have in the past abandoned attempts to correct the male factor and have turned to adoption. However, the adoption patterns of the 1970's

have changed dramatically with the new abortion laws, so that adoptable babies have become difficult to obtain. In view of this, AI presents a viable alternative to the infertile couple. It has been estimated that 10,000 babies are born each year as a result of AI. It is the purpose of this report to present our experience with three cases of artificial in-

semination.

### Material and Methods

Three potential candidates for artificial insemination were referred to our center in order to have an evaluation prior to artificial insemination with frozen semen (Table 1). After they were accepted, the procedure was thoroughly discussed and an informed consent obtained. Donor's frozen semen, collected and processed at Idant's New York laboratory was used in the three cases presented (2).

The semen was used within two or three minutes after its removal from the tank of liquid nitrogen. The patient was prepared for insemination before the frozen semen was withdrawn. After appropriate preparation of the female, excess cervical mucus was removed, leaving a small amount in the cervical os. The inseminator was inserted about 1 cm. in the cervical os. After this, the female subject was inseminated daily, starting two days prior to the anticipated date of ovulation and ending on the day of ovulation.

### Case Presentation

*R. M. M. No. 5910.* Twenty-eight year old female, married for eight years. The husband was previously sterilized and two subsequent plastic operations for recanalization of the vas deferens were unsuccessful. The female partner was a case of anovulatory cycles. She received Clomid for 5 days and human chorionic gonadotrophin (HCG) 10,000 I.U., parenterally the first day of the insemination (3). She was inseminated on three consecutive days. She became pregnant in the first insemination cycle.

A living baby girl, weighing 8 lbs. 5 oz. was delivered at term by C-section due to cephalo pelvic disproportion. Bilateral polycystic ovaries were found during operation and a wedge resection of both ovaries was performed.

At the present she is ovulating and has requested a second insemination attempt.

*R. A. G. E. No. 4963.* Twenty-seven year old

female, married for four years. Her husband was a patient with Klinefelter's syndrome (azoospermic). She knew of her husband's genetic problem prior to her marriage. She also was a case of anovulatory cycle, and received Clomid 50 mgs. daily for five days and H.C.G. 5,000 I.U., I.M. the first day of the insemination.

Inseminations were done on three consecutive days. Clomid was increased to 50 mgs. bid and H.C.G. to 10,000 I.U., I.M. She got pregnant in the second cycle, and delivered twin baby girls 35 weeks later. The first was born in vertex presentation, delivered by low prophylactic forceps after a median episiotomy. She weighed 5 lbs. 4 oz., apgar score 8-9. The second was born several minutes later, by total breech extraction, weighing 4 lbs., 14 oz.; apgar score 8-9. One large placenta and two separated amniotic sacs were obtained.

*M.H.E. No. 7216.* Twenty-seven year old female who had been married for four years. Her husband was a known case of Klinefelter's Syndrome. The first cycle of insemination was done on three consecutive days; H.C.G. 10,000 I.U. was given I.M. the first day of the insemination to pinpoint ovulation. A second cycle was performed nine months later. H.C.G. 10,000 I.U. was given I.M. the first day of the insemination. She had symptoms suggestive of an intrauterine pregnancy 4 to 6 weeks later. She had a positive pregnancy test, but started to notice intermittent vaginal spotting several days later. Repeated pregnancy tests were negative. This was a possible case of early abortion, however objective evidence could not be obtained.

### Discussion

With fewer adoptable babies available in this century, infertile couples in whom the male is a factor in the infertility, must consider artificial insemination (AI), if they are to have children (4). It is, therefore, clear that a large number of infertile couples can be helped and given the satisfaction of raising their own children by AI using frozen semen.

There are many advantages to the use of frozen semen for anonymous donor insemination (5-6):



1. Immediate and convenient access to semen from a diverse group of carefully screened donors of known genetic constitution. This eliminates the inconvenience of last minute calls to donors and the attendant difficulties of proper coordination with the ovulatory stage of the patient's menstrual cycle.
2. Multiple inseminations in a given ovulatory cycle may be done, if desired, enhancing the probability of conception.
3. Access to comprehensive and detailed information with regard to each semen specimen used: blood type, RH factor, sperm count, motility, both before and after freezing, and the results of morphological examination of the spermatozoa of the donor.
4. Tests of the donor's blood and semen for venereal disease and gonococcus are performed routinely, increasing the safety factor for the patient.
5. A detailed profile of the donor is provided, including among other factors; genetic background, somatype, height, complexion, eye and hair color, education level, religion, etc.
6. Cost is comparable to the expense of obtaining fresh semen.

ble time and counsel (8) should be available for couples contemplating the procedure. The two most important aspects of AI are a source of well-screened donor and the timing of insemination with ovulation. Within this context, the use of frozen semen from a bank offers considerable flexibility in dealing with a subject as variable as a woman's ovulatory cycle. Multiple inseminations in a given ovulatory cycle may be done, if desired, enhancing the possibility of conception.

### Fertility Work-Up

No AI should be attempted until the wife's fertility has been exhausted. She should be free from any obvious cervical, uterine or tubal pathology that might result in infertility. Special interest here, of course, is devoted to prove that the tubes are patent and to the timing of ovulation. Tubal patency is confirmed by hysterosalpingography.

### The Donor

The donor should be unknown to the couple. His health and fertility must be impeccable and there should be no family history of genetic disease. His physical proportions should be similar to the husband, and his intelligence at least equal to each of the parents. The Rh factor of the donor must be similar to that of the recipient (8).

### Timing

The biggest single factor in unsuccessful inseminations is the timing of ovulation. Pinpointing ovulation is often difficult in AI, since the patient's emotional status can delay ovulation for a few days. Different authors

Frozen semen has been used to initiate hundreds of pregnancies with the incidence of birth defects not greater, and perhaps, lower than the usual incidence (6). Genetic damage to spermatozoa during the freezing process is a theoretical possibility. Because of the emotional aspect of AI (7), considera-

have recommended administration of estrogen I.V. or H.C.G., I.M. in an effort to insure that ovulation occurs (3). The days selected for insemination are based upon the knowledge of the length of five or more consecutive menstrual cycles, daily basal body temperature (B.B.T.) reading, and cervical mucus smears.

The only true indication for artificial insemination is the psychologically and physiologically normal female, married to a psychologically healthy male who for whatever reason has total azoospermia (10). To this should be added, men with nechrospermia, men with severe oligospermia with infertility of long duration, men with circulatory sperm antibodies, and men with a previous vasectomy (11).

The interview with the patient and her husband is of utmost importance. They must request the procedure, understand the procedure, accept the responsibility for any abnormal or defective child, and accept the offspring as their own. Legal, moral and religious aspects of AI must also be discussed (10).

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## AVISO DE INTERES

La Junta Editora, consciente de su responsabilidad de hacer que el "Boletín" cumpla a cabalidad con su cometido de divulgar conocimientos médicos, elevar las normas de educación médica y al propio tiempo de llenar las necesidades de todos los compañeros médicos, ha acordado establecer una nueva Sección que se conocerá como "Sección de Preguntas".

Bajo esta nueva Sección, todos los compañeros tendrán la oportunidad de enviarnos preguntas médicas de casos difíciles o casos clínicos para opinión experta. Estas preguntas, con sus respuestas, serán publicadas en esta nueva Sección.

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AVAILABLE ONLY ON PRESCRIPTION

### Brief Summary

**INDICATION:** Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect, rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle, the patient should therefore be cautioned accordingly. **Drug Dependence:** Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression, changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. **Use in Pregnancy:** Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. **Use in Children:** Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdose. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* Impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSE AND ADMINISTRATION:** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release. One 75 mg. tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSAGE:** Manifestations of acute overdose include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phentolamine (Regitine®) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdose.

Product Information as of April, 1976

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## **In uncomplicated overweight.**

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

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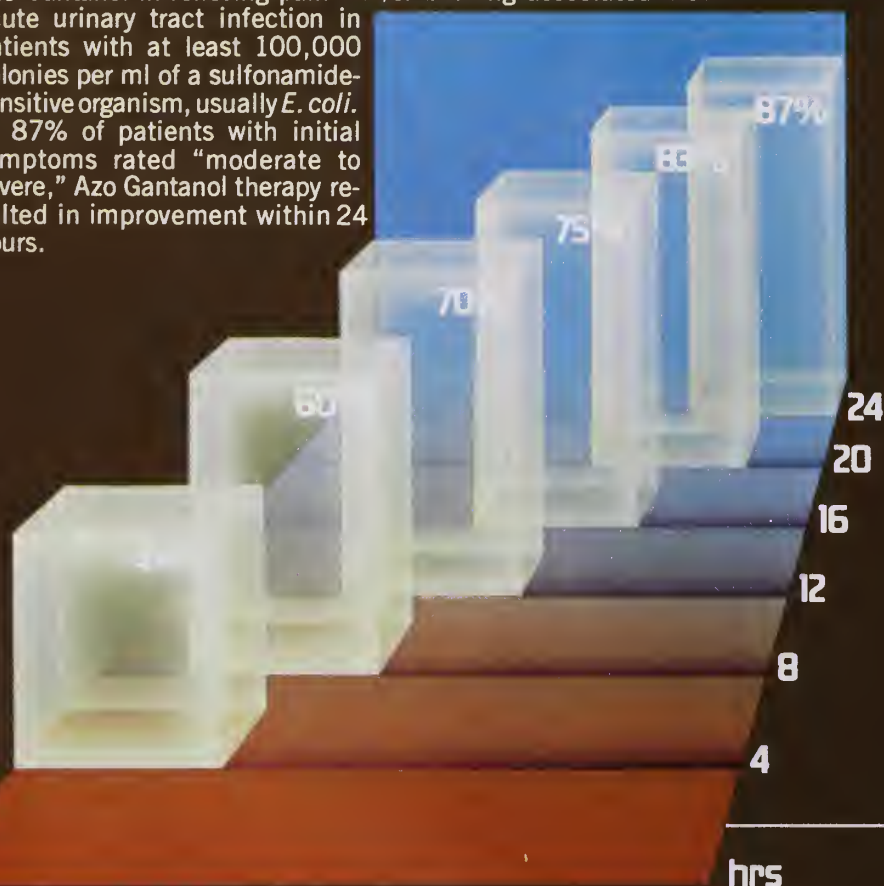


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Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. **Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

**Warnings:** Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** *Blood dyscrasias* (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); *allergic reactions* (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); *G.I. reactions* (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); *CNS reactions* (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); *miscellaneous reactions* (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

**Dosage:** Azo Gantanol is intended for the acute, painful phase of urinary tract infections. *Usual adult dosage:* 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

**NOTE:** Patients should be told that the orange-red dye (phenazopyridine HCl) will color the urine.

**Supplied:** Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500.

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Fast pain relief plus effective antibacterial action

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Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

for  
the pain

for  
the pathogens



### EDUCACION MEDICA EN PUERTO RICO

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*En los últimos años han ocurrido cambios significativos en la Prestación de Servicios de Salud y en los recursos humanos disponibles. Estos cambios están en todo su apogeo y es muy importante que su desarrollo sea ordenado y bien planificado. En el año 1972, un comité de la Escuela de Medicina del Recinto de Ciencias Médicas fue nombrado para estudiar la situación que afectaba a la educación médica y los servicios de salud en Puerto Rico. Su informe titulado "La Educación Médica en Puerto Rico: Bases para Establecer una Política Educativa", fue un excelente análisis de la labor realizada antes de 1950 y de 1950 al 1972. Aquí se expusieron problemas y se sugirieron soluciones a corto y largo plazo. En la publicación de Buhití de marzo de 1973, se presentaron los datos de este cuidadoso análisis. Entre las recomendaciones se encontraba el establecimiento de un Consorcio Educativo en los centros médicos de Ponce, Caguas, Mayaguez y Bayamón, con el propósito de aumentar el número de estudiantes de medicina a graduarse de nuestra escuela, no establecer escuelas privadas y el fortalecimiento del Sistema de Salud con un seguro de salud y mejor distribución de los profesionales de la salud. Se proyectaba que para 1985 habría 5,150 médicos para una relación de médico/habitantes de 1:664.*

*Al 1979 han transcurrido sólo 7 años de este informe y podemos ver cómo en tan poco tiempo se ha actuado en una forma u otra sobre cada punto. Los médicos en el país han provenido principalmente de las escuelas en México y la República Dominicana sin que haya habido control o planificación alguna. Esto ocurrió mientras se instituían 3 nuevas escuelas de medicina privadas para atender una gran demanda de nuestros estudiantes y para poder enfatizar la medicina primaria, supuestamente desatendida por nuestra Escuela de Medicina en San Juan.*

*En 1979, nos encontramos que el número de médicos sobrepasa los 5,150 esperados para 1985 sin aún haberse graduado los primeros estudiantes de las tres escuelas privadas ni el número máximo de 150 graduandos de nuestra Escuela cifra autorizado por el Comité de Enlace de Educación Médica y la Asociación Americana de Colegios de Medicina al crearse el Consorcio Educativo.*

*Estos hechos nos han motivado a hacer un estudio para identificar el número de puertorriqueños que estudian medicina aquí y en el extranjero con el propósito de hacer nuevas proyecciones para el año 1984. Los datos del Registro de Profesionales de la Salud nos darán un número bastante exacto de los médicos en práctica activa al presente.*

*La gran preocupación que existe es si con el número significativo de estudiantes de medicina en Puerto Rico y en el extranjero habrá un exceso de proveedores en el futuro cercano. La contestación es en la afirmativa. Es muy probable que todos los 600 estudiantes puertorriqueños que de-*



sean estudiar medicina anualmente tengan cabida en las universidades, especialmente en el extranjero. Algunos de estos estudiantes no tienen credenciales para estudiar medicina.

En la controversial Ley de Reforma a la Ley Número 22 se provee para 3 requisitos de pre-médica para tomar los exámenes del Tribunal Examinador de Médicos. Se requerirá un índice mínimo de 2.5, no menos de 90 créditos de pre-médica y haber cogido un examen de aptitud médica (MCAT). La importancia de estas medidas ha sido ignorada por otras de menos trascendencia en mi opinión.

Nos toca ahora planificar los programas y oportunidades a ofrecerse a los nuevos profesionales con cuidado y reconocer a tiempo cuando ha llegado al número óptimo que necesita el país. Estamos conscientes que si pocos médicos es malo muchos puede ser peor. Esperamos que las agencias gubernamentales y la Asociación Médica nos ayuden a través del Comité Asesor del Recinto de Ciencias Médicas a poder orientar a nuestros jóvenes y sus padres. Los oficiales de las escuelas de medicina del país deben estar atentos y acoplar sus planes a nuestras realidades.

Norman I, Maldonado, MD

#### CONTESTACIONES: (A)

1. E
2. A, F
3. G
4. B, H
5. D
6. D
7. B
8. C
9. A

## LA REGIONALIZACION MEDICA EN PUERTO RICO

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El Dr. Guillermo Arbona recibió recientemente la distinción de Profesor Emeritus del Recinto de Ciencias Médicas de la Universidad de Puerto Rico. El fue uno de los principales arquitectos junto al fenecido Dr. John B. Grant, en el desarrollo del Sistema de Salud Pública en Puerto Rico.

En su reciente libro "Regionalization of Health Services, The Puerto Rican Experience", el doctor Arbona y la Sra. Annette B. Ramírez de Arellano hacen un recuento histórico del desarrollo del Sistema de Prestación de Servicios de Salud en Puerto Rico y su evolución a un Sistema de Regionalización (concebido en 1947 hasta sus más recientes cambios en 1977). En este libro se hace un magnífico análisis de las causas para que el sistema, aunque con ciertos logros, no funcionara a cabalidad, a pesar de que conceptualmente parece ser la mejor alternativa para bregar con los problemas que acarrea la prestación de servicios de salud a nuestro pueblo. De estas experiencias podemos aprender mucho, no tan solo nosotros, sino otros países que aún no tienen sistemas de salud establecidos.

En Puerto Rico, al igual que en otros países, co-existen varios sistemas de salud atendiendo a distintos grupos poblacionales. El sistema gubernamental atiende un 60 por ciento de la población, y el sistema de práctica privada entre el 30 por ciento y 40 por ciento. En adición, el Fondo del Seguro del Estado presta servicios a sus asegurados y la Administración de Veteranos a los veteranos del ejér-

cito de los Estados Unidos. Existen varios planes médicos que son parte del sector privado. Todos sabemos que hay un flujo de pacientes que cruzan de un sistema a otro por razones de conveniencia económica o para conseguir una más pronta atención. Estamos seguros que aquí ocurre duplicidad de esfuerzo y costos innecesarios, al igual que sobre tratamiento en algunos núcleos poblacionales.

El Sistema de Prestación de Servicios de Salud Regionalizado ha tenido en el pasado oposición por parte de la alta jerarquía dentro del Departamento de Salud Central, como por algunos miembros de las clases profesionales, especialmente la Asociación Médica de Puerto Rico a través de los últimos treinta (30) años.

En los últimos años se ha realizado un gran esfuerzo por fortalecer el Sistema de Prestación de Servicios de Salud Gubernamental, desarrollando equipos de salud en los niveles primarios, estableciendo el concepto de área y mejorando las facilidades a nivel terciario, especialmente con la acreditación de los hospitales regionales y centros médicos.

Al igual que no podemos decir que el Sistema de Regionalización ha sido un factor importante en la mejor salud de nuestro pueblo, tampoco podremos predecir el impacto que tendrán los cambios que han ocurrido en las estadísticas vitales durante los últimos años. Sin embargo, es de esperarse que la población se sienta más satisfecha cuando acude a las facilidades gubernamentales en búsqueda de

cuidado médico o de primeros auxilios. La ley que dispone para el servicio público por parte de los médicos y de todos los demás profesionales de la salud, será probablemente el factor más importante en el mejoramiento de estos servicios y en la re-vitalización del Sistema de Regionalización Médica de Puerto Rico.

El viernes 21 de septiembre se inauguró el Hospital de Area de Yauco con un nuevo concepto de prestación de servicios de salud. Esta moderna facilidad totalmente equipada servirá a las poblaciones de Guayanilla, Peñuelas, Guánica y Yauco, como un hospital de área donde se atenderán los pacientes referidos de estas cuatro poblaciones y cualquier otro ciudadano que necesite servicios de salud. La operación de esta institución es una integración del gobierno con la comunidad y con la medicina privada del país. Este será el primer hospital en Puerto Rico que, perteneciendo al gobierno, será adminis-

trado por una junta de gobierno que representa la comunidad. Todos los empleados, comenzando por el Director Ejecutivo, incluyendo los profesionales de la salud y los médicos serán empleados o trabajarán bajo contrato de la Junta de Directores. Los servicios médicos serán provistos por grupos de profesionales médicos en las distintas disciplinas que atenderán a los pacientes médico-indigentes, por los cuales el estado pagará sus gastos y todos los pacientes que tengan recursos económicos o planes médicos serán atendidos en igual forma.

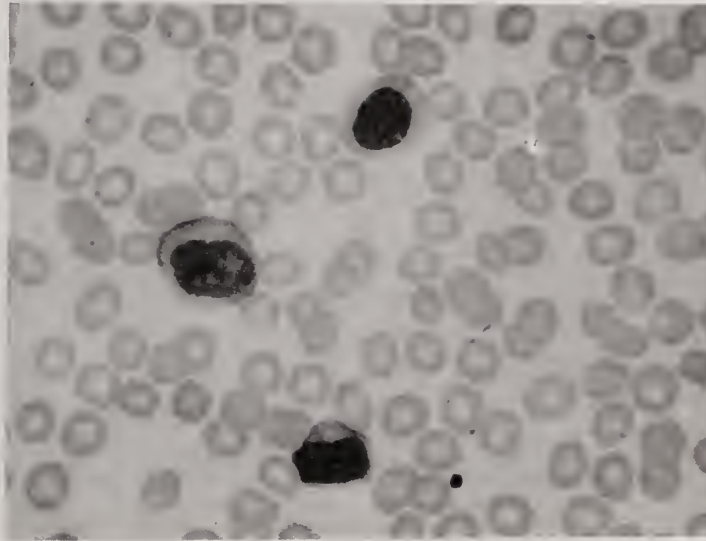
Este experimento, el cual es el primero en llevarse a la realidad, sentará las pautas para lo que pudiera ocurrir en Puerto Rico, de establecerse un seguro de salud nacional como se especula que ocurrirá a principios de la década del ochenta.

*Norman Maldonado, MD*



## G R A P H I C S

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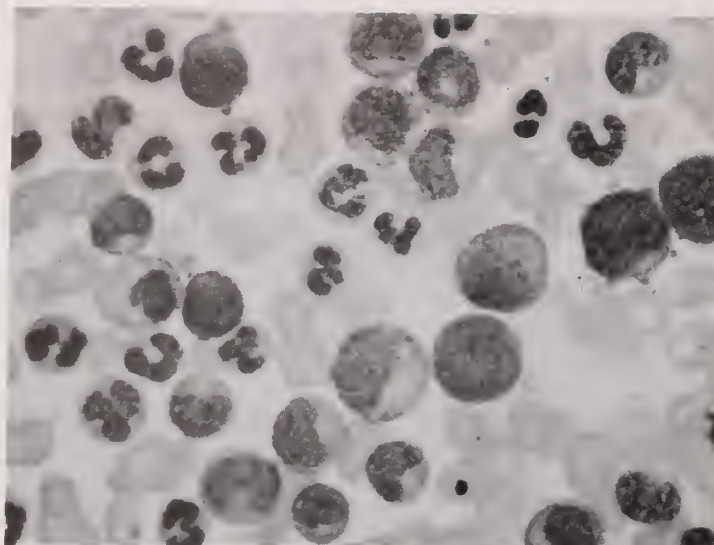
### Case 1:

This 16 year-old patient was seen because of fever, anorexia and enlarged cervical nodes for the past 10 years. He was treated with Penicillin with no response. A throat culture grew staphylococcus albus.

On physical examination he had slight facial swelling and a faint maculopapular rash over the face and trunk. The sclerae was slightly icteric. The tonsils showed a whitish membrane. The cervical, axillary and inguinal nodes were enlarged. The liver was palpable and the spleen was also felt 2cm below the costal margin.

The Hgb was 10gm., WBC 18,000 platelet count 160,000. The most likely diagnosis is:

- a) Hodgkins Disease III B
- b) Hodgkins Disease IV B
- c) Acute Viral Hepatitis (Type A)
- d) Infectious Mononucleosis
- e) Diphtheria

**Case 2:**

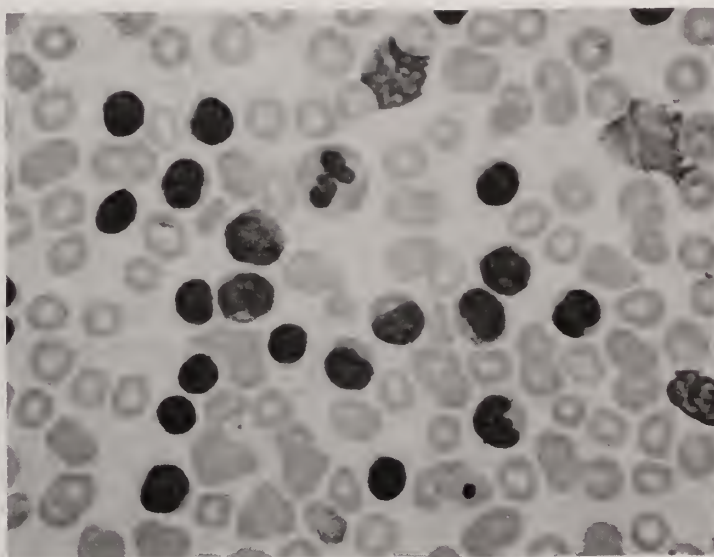
This 40-year old mother of 2, presents with early satiety and weight loss. She has had night sweats and claims to have pounding of her chest when she climbs a flight of stairs. Pain in the right elbow has been present for about 1 week with no relief from standard analgesics.

On physical examination she is slightly pale. There are no adenopathies. The spleen is felt 6cm below the costal margin. The liver is felt 2cm below the costal margin. The right elbow is very tender to palpation.

The Hgb is 10.5 gm, WBC 130,000, platelet count 480,000.

The likely diagnosis:

- a) Miliary Tuberculosis
- b) Leukemoid reaction
- c) Myelofibrosis and Myeloid metaplasia
- d) Acute Granulocytic Leukemia
- e) Chronic Granulocytic Leukemia



**Case 3:**

A 60-year old man was seen by his cardiologist on a routine visit. He was found to have generalized lymphadenopathy. He was asymptomatic. The physical examination confirmed cervical, axillary and inguinal adenopathies ranging from 1 to 2cm. and rubbery in consistency. The liver was felt 4cm. and the spleen 6cm. below the costal margins. The Hgb was 14gm. WBC 100,000, the platelet ct 120,000.

- a) Acute lymphatic Leukemia
- b) Blastic crisis of CGL
- c) Chronic Lymphatic Leukemia
- d) Infectious Lymphocytosis
- e) Burkitts' Lymphoma



## Case 1:

This patient has classical Infectious Mononucleosis. The jaundice can be due to liver involvement that is always reversible or to hemolytic anemia. In this patient the Coombs-Test was positive and the reticulocyte count 15 percent which means that the anemia is due to antibodies. This is seen in some cases of I.M.

The patient was treated with Prednisone 60mg. daily and had a prompt response of the anemia and the other symptoms.

## Case 2:

This patient has Chronic Granulocytic Leukemia. The leukocyte alkaline phosphatase was zero. There was a  $Ph^1$  chromosome in the bone marrow karyotype to confirm the diagnosis. The uric acid was 12mg. percent and she had secondary gout.

Treatment with Benemid, Zylprim and Myleran (busulfan) was started. In 3 months she was in complete remission and the Benemid and Zylprim were discontinued.

## Case 3:

This patient has chronic lymphatic leukemia. She was found to have hypogammaglobulinemia with low immunoglobulin G. It was decided to treat her with Leukeran (Chlorambucil) and Prednisone. She went into remission in 6 months.

## CONTESTACIONES: (B)

1. E, F, G

2. E, D

3. C, G

4. A, B

### FALTA DE EVIDENCIA PARA ASOCIAR AL CANCER CON EL USO DE METRONIDAZOLE (FLAGYL®)

C. M. Beard, et al. New Eng. J. Med. 301: 519-522, 1979.

El uso de metronidazole ha estado siendo cuestionado debido a que experimentos demostraron que este agente era carcinogénico a roedores y mutagénico a las bacterias. Un estudio de 771 mujeres que recibieron metronidazole (Flagyl®) para tratamiento de trichomoniasis vaginal reveló que el número de cánceres vaginales, de mama y pulmón no excedían lo que se esperaba.

El estudio ofrece información valiosa sobre la falta de asociación entre cáncer y metronidazole en humanos. Los roedores son diferentes a los humanos, más otros datos después de administración sistémica y parenteral deben esperarse.

(Sometido por Carlos H. Ramírez Ronda, MD, VAH)

### HISTORIA NATURAL DE BACTERIURIA EN NIÑAS DE EDAD ESCOLAR: UN ESTUDIO A LARGO TIEMPO CON CONTROL DE CASOS.

J. Y. Gillenwater, R. B. Harrison y C. M. Kunin, New Engl. J. Med. 301: 396-399, 1979.

Bacteriuria en las niñas de edad escolar es frecuente, su significado pronóstico e implicaciones clínicas no están claro. Este estudio define mejor la

historia natural de bacteriuria en las mujeres. Los autores siguieron 60 niñas de edad escolar con bacteriuria y 38 controles balanceados por períodos de 9 a 18 años. Entre las niñas de edad escolar con bacteriuria, definida como urocultivos positivos con más de  $10^5$  microorganismos por mililitro en dos o más urocultivos consecutivos, se reparó reflujo en 5, se realizó nefrectomías en dos y se apuntó una reducción en la depuración de inulina en un sujeto con pielonfritis atrófica. La creatinina sérica fue ligeramente más elevada en los casos que en los controles. Cicatrices renales o caliectasis ocurrió en 16 casos más en ninguno de los controles. La presión sanguínea fue similar en ambos grupos. Los episodios de bacteriuria en los casos y los controles fueron respectivamente: cinco o más episodios, 21.7 y 2.6 por ciento, y episodios durante el embarazo 63.8 y 26 por ciento. A siete niñas de los casos y ninguno de los controles se le encontró infección del tracto urinario. Bacteriuria en niñas de edad escolar define un grupo de personas (mujeres) que están a un riesgo más alto de infecciones recurrentes sintomáticos y cicatrices renales y a un riesgo bajo de función renal reducida.

Sometido por Carlos H. Ramírez Ronda, MD, VAH)

### USO DE DROGAS ANTIMICROBIANAS EN HOSPITALES GENERALES

M. Shapiro, T. R. Townsend, B. Rosner, y E. H. Kass. New Eng. J. Med. 301: 351-355, 1979.

Los patrones de uso de antibióticos en 20 hos-

pitales en Pennsylvania fueron estudiados. Los patrones de uso profiláctico de antibióticos se obtuvo revisando 5,288 expedientes médicos. El 10 por ciento de los pacientes hospitalizados recibieron antibióticos profilácticamente en operaciones o procedimientos no-quirúrgicos, y el uso de antibióticos profilácticamente fue responsable del 30 por ciento de todos los antibióticos administrados en los hospitales. Las drogas que se utilizaron más frecuentemente fueron cefalosporinas, seguidas por benzyl penicilinas, ampicilina y tetraciclina. A pesar de que las indicaciones de que profilaxis, cuando es útil, es solamente efectivo cuando se administra concurrentemente con y por 24 a 48 horas después de la operación se utilizó usualmente durante todo el período de hospitalización. Casi el 80 por ciento de los agentes utilizados profilácticamente se administraron por 48 horas o más después de la operación.

El uso profiláctico de antibióticos en procedimientos quirúrgicos está bien definido. El uso en situaciones no-efectivos constituye un riesgo para el paciente y un aumento en los costos de hospitalización. Cuando su uso está indicado no debe de exceder 48 horas.

Véase también el editorial: Antibiotic Accountability, C. M. Kunin - New Eng. J. Med. 301: 380-381, 1979.

(Sometido por Carlos H. Ramírez Ronda, MD, VAH)

### VALVE REPLACEMENT FOR AORTIC REGURGITATION: LONG-TERM FOLLOW-UP WITH FACTORS INFLUENCING THE RESULTS

Samuels, D. A., Curfman, MD, Friedlich, MD, Buckley, MJ, Austen, WG. Circulation 60: 647, 1979.

En este estudio se analizan 100 casos de reemplazo de válvula aórtica debido a regurgitación aórtica. Ochenta y tres pacientes sobreviven la operación y de éstos 78

por ciento quedan asintomáticos. Los factores que mejor indicaron a los pacientes con buen resultado de cirugía fueron: severidad y duración de la dysnea, intensidad de la terapia médica para fallo congestivo, cardiomegalia en radiografía de pecho, presión en cuña pulmonar e índice cardíaco. Concluyen los autores que cualquier evidencia de fallo de ventrículo izquierdo, no importa cuán de leve, es indicación para cirugía en pacientes con insuficiencia aórtica severa.

(Sometido por Guillermo Cintrón, MD)

### SEMIMEMBRANOUS INSERTION SYNDROME: A TREATMENT AND FREQUENT CAUSE OF PERSISTENT KNEE PAIN

Weiser, Hans I, MD - Arch Phys Med Rehab 60: 317-319, 1979

El síndrome de la inserción semimembranosa causa dolor en el aspecto medial de la rodilla. Este dolor se empeora con el ejercicio, al bajar escaleras o en flexión brusca de la rodilla. El paciente experimenta dolor y palpación, hinchazón moderada en la porción más inferior de los (Hamstrings) mediales y dolor en la rotación pasiva de la rodilla. Si se presiona con el dedo la inserción del tendón semimembranoso se produce un dolor agudo.

Tratamiento con calor o ejercicios agrava el dolor. Un ciento de pacientes con este síndrome se trataron con inyección local de lidocaína con triamcinolone, lográndose de inmediato un alivio temporero. Alivio más duradero se consiguió en 58 pacientes, en 30 de los cuales fue necesario repetir la inyección en 3-5 meses. En 9 pacientes disminuyó el dolor y mejoró su incapacidad. En 18 el seguimiento fue un fracaso y en 15 pacientes no hubo seguimiento.

(Sometido por Verónica Rodríguez, MD, VAH)

### CARDIAC SURGERY DURING THE FIRST YEAR OF LIFE AT THE UNIVERSITY OF



## PUERTO RICO SCHOOL OF MEDICINE

Víctor N. Ortiz, MD, Mercedes Vega Vidal, MD, and Enrique Márquez, MD - from Sections of Pediatric Surgery and Cardiology, University of Puerto Rico, School of Medicine.

From 1973-75 (24 months), 193 Pediatric Cardiovascular cases were done. 75/193 (40 percent) were 12 months old, 14/75 (18 percent) had 2 or more significant cardiac diagnoses, making a grand total of 89 diagnoses. Male to female ratio was 2:1. 26/75 (34 percent) were 1 month old, the largest group. Our mortality rate was 22 percent, the seven commonest diagnoses were: P. D. A.; T. F.; V. S. D.; T.G.V.; T.A.; Co.Ao.; and Pulmonary Stenosis and/or atresia. They constituted 80/89 (90 percent) diagnoses). *T.A.* and *T.G.V.* had the largest mortality rate: 33 percent on each group. Our mortality is lower than most of the largest series in U. S.; most of these series have twice the patients per year than ours. Improved surgical (loops, suture material, etc.) and anesthesia techniques; together with aggressive multidisciplinary team approach to the management of the pre and postop problems that might arise, are the reasons for the above results.

## TEAM APPROACH TO THE MANAGEMENT OF SOLID ABDOMINAL TUMORS IN CHILDREN

Víctor N. Ortiz, MD, Irma Ramírez, MD, Pedro J. Santiago, MD and Enrique Márquez, MD - from the Sections of Pediatric Surgery and Hematology-Oncology, University of Puerto Rico, School of Medicine.

40 patients, diagnosed from 1971-73 (24 months) are presented: 1) 12/40 (30 percent)-Wilms; 2) 12/40 (30 percent)-Neuroblastoma; 3) 11/40 (28 percent) - lymphosarcoma; 4) 3/40 (7 percent)- Hepatoblastoma; 5) 2/40 (5 percent) - miscellaneous. In the Wilms group 11/12 presented with a palpable abdominal mass. Currently, 7 are alive and well and 5 have died. (Stage III

or IV). In the Neuroblastoma group, 2 were benign (ganglioneuroma) both alive and well. Of the other 10 patients: 9 are alive but only 3 are well (= free of disease); 1 dead. In the lymphosarcoma group: 6 are alive and 5 died. Lymphomas was the largest subgroup (5) and rhabdomyosarcoma next (4). 3 Lymphoma's patients were Burkitt's and all died. In the hepatoma group one is alive and well after lobectomy. Recognition, identification and treatment of these patients must be done in a Pediatric Center capable of handling all possible diagnoses and complications that might arise, expeditiously.

## HISTORY AND MANAGEMENT OF HIRSCHPRUNG'S DISEASE AT THE UNIVERSITY HOSPITAL OF PUERTO RICO

Víctor N. Ortiz, MD, and Enrique Márquez, MD, Department of Surgery, University of Puerto Rico, School of Medicine

Forty patients having pull-thru(s) from 1965 - 75 are presented. All histopathologically proven. True pos. without definitive surgery; and false pos., with or without definitive surgery will be discussed. Our 1968 series will serve for reference. 75 percent (30/40) were diagnosed < 6 months old. (mean: 25 days). All 30 had Pull-thru(s) < 16 months old. 70 percent (21/30) presented with constipation; and 30 percent (9/30) with Enterocolitis, 25 percent (10/40), were diagnosed > 6 months old. ( mean: 2.8 years). 100 percent (10/10), presented with constipation. 10 patients are lost to follow up.. 25 out of 30, were Soave's; 3 Swenson; and 2 Duhamel Pull thru(s). In the Soave's group: mortality was 1/25 - unrelated to surgery; total short term complication number was 12, related to surgery. Wound infection total number was 6. Follow up in the Soave's group (mean: 42 months) showed 5 long term complications: constipation in 2 and incontinence in 3. We have improved in *earlier diagnosis and treatment*, due to increased awareness by referring physicians. Early results with our Soave's pull-thru(s) are excellent. Postop follow up must, and is being improved. Objec-

## NOTA DEL EDITOR

tive, systematic studies (manometry, fecograms, etc.) and prolonged follow up is required for critical analysis. A film of our Soave's technique will be presented.

Estos abstractos fueron presentados en la Sesión Científica de la Asociación Médica de Puerto Rico celebrada en Noviembre 1975. Debido a un error involuntario, no fueron publicados en el Boletín correspondiente.



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in single-dose vials  
and in 8 ml. multiple-dose vials,  
both in packages of 10.

**SK&F LAB CO.**  
a SmithKline company



**When painful spasm  
is the presenting  
symptom...**



...in the functional bowel/irritable bowel syndrome\*

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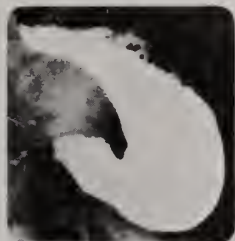
10 mg. capsules, 20 mg. tablets,  
10 mg./5 ml. syrup, 10 mg./ml. injection

helps control abnormal motor activity  
with minimal anticholinergic side effects†

**Demonstrated smooth muscle relaxant activity.**

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

*“The correlation of spasm relief and drug given was excellent.”*

\*This drug has been classified “probably” effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:

King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

# Merrell

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Brief Summary

### INDICATIONS

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

**CONTRAINDICATIONS:** Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with: Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur.

**ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia, urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis; urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

**Usual Dosage:** Bentyl 10 mg. capsule and syrup: *Adults:* 1 or 2 capsules or teaspoonfuls syrup three or four times daily. *Children:* 1 capsule or teaspoonful syrup three or four times daily. *Infants:* ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg.: *Adults:* 1 tablet three or four times daily. Bentyl Injection: *Adults:* 2 ml. (20 mg.) every four to six hours intramuscularly only. **DO NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine<sup>®</sup> (bethanecol chloride USP) should be used.

Product Information as of October, 1978.

Injectable dosage forms manufactured by CONNAUGHT LABORATORIES, INC., Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Decatur, Illinois 62525 for MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215, U.S.A.

# Merrell

MERRELL-NATIONAL LABORATORIES  
Division of Richardson-Merrell Inc.  
Cincinnati, Ohio 45215 U.S.A.



*THE AMERICAN COLLEGE OF CARDIOLOGY and  
THE LANKENAU HOSPITAL, Philadelphia, Penn.  
announce*

CROSS SECTIONAL ECHOCARDIOGRAPHY  
VS.  
CARDIAC NUCLEAR IMAGING

December 12, 13 and 14, 1979

To be presented at:  
FAIRMONT HOTEL  
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*THIRD PEDIATRIC NEPHROLOGY SYMPOSIUM  
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TER announce*

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Program Director:  
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*THE AMERICAN COLLEGE OF CARDIOLOGY  
announces EXTRAMURAL PROGRAMS IN CON-  
TINUING MEDICAL EDUCATION - January 1980  
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Jan. 14-18 Eleventh Annual Cardiovascular Confer-  
ence at Snowmass, Snowmass, Colo.

Jan. 15 Coronary Artery Disease: Diagnosis and  
Treatment, San Antonio, Tex.

Jan. 31 Fundamentals of Echocardiography — An  
Feb.2 Introductory Course for Clinicians, Los  
Angeles, Calif.

Feb.13-15 Cardiovascular Disease-1980: Advances

in Diagnosis and Management, San Diego, Calif.

Mar.24-28 Electrocardiographic Interpretation of Complex Arrhythmias: A Physiological Approach, Indianapolis, Ind.

Apr.7-16 Cardiology for the Consultant: A Clinician's Retreat, Rancho Santa Fe, Calif.

Apr.10-13 Current Concepts and Advances in Diagnosis, Management and Prevention of Cardiac and Cardiopulmonary Diseases, Los Angeles, Calif.

Apr.14-18 Consultant's Course in Cardiology, New York, N. Y.

Apr.16-18 Vectorcardiography—Basic Workshop, Scottsdale, Ariz.

Apr.21-23 Practical Cardiology for the Family Physician, San Antonio, Tex.

Apr.24-26 The Pathology of Congenital Heart Disease, Chicago, Ill.

Apr.25-27 New Concepts in Clinical Electrocardiography, Beverly Hills, Calif.

May 1-3 Problems in Management of Valvular and

Ischemic Heart Disease, Tarpor Springs, Fla.

May 3-6 A Symposium on Cardiovascular Nursing, Miami Beach, Fla.

May 7-9 Diagnosis and Treatment of Dysrhythmias in Children, Houston, Tex.

May 7-9 Clinical Auscultation of the Heart, Washington, D.C.

May 12-14 Trends in Cardiology, Atlanta, Ga.

May 15-17 Acute Myocardial Infarction, San Francisco, Calif.

June 5-7 Cardiovascular Nuclear Medicine and Comparative Techniques 1980, New Haven, Conn.

June 9-11 Frontiers in Coronary Artery Disease, Newport, R. I.

June 11-14 Clinical Echocardiography: Fundamentals and New Developments in Cardiac Ultrasound, San Diego, Calif.

Aug.23-25 Tutorials in the Tetons: Cardiac Emergencies (Sixth Annual), Moran, Wyo.

## *BACKGROUND: THE MANAGEMENT OF RISK FACTORS IN CARDIOVASCULAR AND RENAL DISEASE*

A blood pressure reading.... a simple history .... an ECG .... a blood test for cholesterol, sugar and uric acid .... a count of cigarettes smoked daily. Basic laboratory tests and ordinary procedures like these are helping physicians develop coronary risk profiles on their patients and making possible more precise estimates of heart disease risk.

For the last three decades, medical researchers have been identifying and studying a growing number of characteristics commonly seen in patients with cardiovascular and renal disease. They call them "risk factors," and their presence puts an individual at greater risk of developing diseases that affect the heart, brain and kidney.

Although blood pressure is the dominant contributor to the incidence of cardiovascular disease, there is a synergistic effect of a number of factors associated with the disease. These include glucose, lipid and uric acid levels in the bloodstream; relative weight; sodium intake; personality and lifestyle.

Much of the available data on cardiovascular disease and associated risk factors have been obtained from the Framingham Study which began in 1949 in Framingham, Massachusetts, and involved more than 5000 men and women, aged 30 to 62. Each of these individuals received a complete physical checkup every two years over a 20-year period.

Statistical analysis of the Framingham data revealed that several risk factors exist in a high percentage of patients with cardiovascular disease. Hypertension—defined as sustained blood pressure readings greater than 140/90 mmHg. — was the leading risk factor. In people between the ages of 54 and 64 with blood pressure of 160/95 mmHg., coronary artery disease

was found three times as often as in patients with normal blood pressure. Stroke was seven times more common in these hypertensive patients.

The Framingham Study also indicated that risk factors are cumulative; the presence of multiple risk factors may increase the risk of developing cardiovascular disease.

Researchers now classify risk factors as "primary" or "secondary," and differentiate between those that can be modified or controlled and those which cannot. Modifiable risk factors can usually be altered through change of lifestyle or diet, or they can be controlled by drug therapy. Generally speaking, these factors include hypertension, obesity, cigarette smoking, elevated blood sugar levels (hyperglycemia), elevated blood cholesterol levels (hypercholesterolemia), and elevated serum uric acid levels (hyperuricemia).

Other factors that may place a person at greater cardiovascular disease risk, which are obviously beyond control, include the patient's sex (men are at higher risk than women), race (higher incidence in blacks than in whites), age (incidence increases with years), and family history (the condition is seen frequently in some families).

Medical researchers recommend that the physician identify all risk factors present in a patient and then monitor and treat as many known factors as possible. In many cases, treatment of one risk factor may be insufficient, or may be complicated by the presence of other factors.

### *Hypertension: A Disease and a Risk Factor*

Considered as a separate disease, hypertension is an insidious killer. More than 35 million Americans are said to have definite high blood pressure. With treatment, their life expectancy does not differ ma-



terially from the normal population. As evidence of this, there has been a significant decline in stroke and coronary disease deaths during the past six years since the National High Blood Pressure Education Program began. Deaths from hypertension-related diseases during this period have declined sharply. Even so, less than half of America's hypertensive patients are estimated to be taking medication for their disease and only about a quarter of them have the disease well controlled.

*Elevated Serum Uric Acid: Signal of Potential Cardiovascular Disease*

Uric acid is a metabolic waste product that is normally excreted through the kidneys. Overproduction or underexcretion of uric acid can cause a buildup of urate in the bloodstream.

Elevated serum uric acid has often been reported in the medical literature and has traditionally been associated with gout and kidney disease. Many physicians believe uric acid may play a role in the development of cardiovascular disease, although that role is uncertain and as yet undefined. The Framingham Study indicated that persons with elevated uric acid levels are at greater risk of developing cardiovascular disease than subjects with normal levels. Several researchers have also found a higher prevalence of elevated serum uric acid in patients who have had myocardial infarctions (heart attacks) than in normals.

A strong association between elevated serum uric acid and hypertension has also been noted. Recent findings indicate that 20 to 40 percent of individuals with untreated hypertension have elevated uric acid levels, as compared to four percent of individuals without hypertension. In addition, the National Heart, Lung and Blood Institute's *Task Force on Blood Pressure Control in Children* found that an elevated serum uric acid level in an otherwise normal individual is one of several factors associated with later development of hypertension, although it is unknown at present whether the elevated serum uric acid level is a cause of the hypertension.

*FIBER OF LEG MUSCLES CONTROLS RUNNING ABILITY*

CHICAGO — Why is it that the half back can put on a blinding burst of speed in that 40-yard sprint for the goal line? It's the "fast-twitch" muscle fibers in his legs.

And why is it that the marathon runner can pound more than 25 miles around the course and finish well ahead of the pack? It's his "slow-twitch" muscle fibers.

Of course, it isn't this simple. But a report in the Medical News Section of the Journal of the American Medical Association of Oct. 19 says that the predominance of one or the other of two muscle fiber types does seem to be a part of winning races.

Researchers at Ball State University are studying the fiber composition of leg muscles and how this affects a runner's chances for top-level competitive success. The researchers took small samples of muscle tissue from the legs of well-trained runners and from non-runners. It has been known for a decade that human muscle is composed of at least two fiber types, usually called slow-twitch and fast-twitch, according to rate of contraction and other characteristics.

Dr. David L. Costill, himself a marathoner and a professor of physical education and biology and director of the Ball State Human Performance Laboratory, found that runners who are successful in long-distance events apparently have more slow-twitch than fast-twitch fibers in their muscles. The leg muscles of sprinters, on the other hand, are made up mostly of fast-twitch fibers.

The ratio of fibers is not changed by training, Dr. Costill found. He is quick to add that many other factors determine whether a runner will be a champion. There are other physical requisites, and coaching and training are vital.

---

*ROLLER COASTER RIDE BLAMED FOR STROKE*

CHICAGO — Riding a high-speed roller coaster

can cause a stroke, says a report in the Oct. 19 Journal of the American Medical Association.

Drs. Max S. Scheer and Daniel J. Carlin of Morristown, N. J., describe the case of a 13-year-old girl who suffered a stroke while riding a roller coaster in which the participants are upside down during part of the ride.

The child was too small for the U-shaped safety bar collar that is lowered over the shoulders of the rider to prevent falling out when upside down, say Drs. Scheer and Carlin. She plunged against the collar, and suffered a compression of the carotid artery. She suffered partial paralysis of one side and impaired speech. The paralysis cleared with treatment and speech improved, with only occasional word blocking remaining a week later.

The problem is that the safety apparatus is designed to fit the average-size person, and the child was small, they say. The girl's neck was forced against the support collar, producing a shock to the left carotid artery and causing formation of a clot that reached the brain.

---

#### *DOCTORS ALERTED TO NEW CAUSE OF RINGWORM*

CHICAGO — Doctors were alerted this week to watch for a new form of ringworm that does not show up under fluorescent light examination, the traditional diagnostic tool for the common scalp in-

fection.

In the past most ringworm was caused by organisms known as the *Microsporum* sp, *M. audouinii* and *M. Canis*. But in the 1950s another causative organism, *Trichophyton tonsurans*, was introduced into the southern and southwestern states from Puerto Rico and Mexico, says a report in the Oct. 19 Journal of the American Medical Association.

Elena Provost of Medical University of South Carolina, Charleston, reports on ringworm statistics gathered at the University from 1973 to 1978 which indicate a dramatic change in the agents causing the fungus infection. In the 1950s, *trichophyton tonsurans* was found only rarely. But in the 1970s it was causing more than 90 per cent of the cases.

The problem is that when the child is brought to the doctor with a scalp infection, the doctor is likely to conduct the fluorescent light examination. If this fails to show ringworm, the diagnosis may be impetigo or some other ailment, and the treatment will be useless for ringworm.

For unexplained reasons, the new type of infection occurs most often in black children. Girls are as likely to be infected as boys. Diagnosis usually requires a laboratory culture study of scalp scales and infected hair roots, Ms. Provost says.

In an accompanying editorial in the same issue, Andrew H. Rudolph, M. D. of Baylor College of Medicine, Houston, traces the history of ringworm in the past generation in the United States, and concludes:

"With the increasing incidence of scalp infections caused by this organism, it is important that the physician consider *T. tonsurans* as a possible agent in the evaluation of any condition involving hair loss, scaling, or inflammation of the scalp."

M E D I   Q U I Z

## (A) – AGENTES ANTI-ARRITMICOS

- |                                 |  |
|---------------------------------|--|
| 1.    Quinidina                 | A. <i>Tiene propiedades antiarrítmicas, se elimina principalmente por el riñón.</i>                              |
| 2.    Disopiramida<br>(norpace) | B. <i>Se metaboliza en el hígado rápidamente al ser administrada por vía endovenosa.</i>                         |
| 3.    Phenytoin<br>(dilantin)   | C. <i>Se metaboliza en el hígado a NAPA, compuesto con propiedades antiarrítmicas.</i>                           |
| 4.    Propranolol               | D. <i>Parecida a lidocaína, se puede administrar por vía oral</i>  |
| 5.    Tocainide                 | E. <i>Este compuesto puede disminuir la depuración renal de digoxina y aumentar el nivel sérico de digoxina.</i> |
| 6.    Mexilistene               | F. <i>Puede producir retención de orina, tiene menos efectos adversos en el sistema gastrointestinal.</i>        |
| 7.    Lidocaine                 | G. <i>Acelera acción de enzimas hepáticas.</i>   |
| 8.    Procainamide              | H. <i>Puede disminuir la síntesis de <math>T_4</math></i>  |
| 9.    NAPA                      |  |

Puede haber más de una contestación – CONTESTACIONES (A) página 348



## M E D I   Q U I Z

### (B) – BLOQUEADORES BETA ADRENERGICOS

- |                       |   |
|-----------------------|---|
| 1. <b>Practalol</b>   | A. <i>Agente bloqueador beta adrenérgico no selectivo, sin actividad simpatomimética.</i> |
| 2. <b>Metoprolol</b>  | B. <i>Aprobado como agente anti-hipertensor, antiarrítmico y antianginoso.</i>            |
| 3. <b>Acebutalol</b>  | C. <i>Agente bloqueador beta adrenérgico con actividad simpatomimética.</i>               |
| 4. <b>Propranolol</b> | D. <i>Aprobado solamente como agente anti-hipertensor. Dosis inicial 50 mg bld</i>        |
|                       | E. <i>Agente bloqueador adrenérgico selectivo a receptores Beta<sub>1</sub></i>           |
|                       | F. <i>Polyserositis y problemas óculo-cutáneos</i>  |
|                       | G. <i>Agentes bloqueadores Beta adrenérgicos no aprobados en la actualidad por FDA</i>    |

Puede haber más de una contestación – CONTESTACIONES (B) Página 354

# Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

## Counting Calories Vital to Dieting

### Calories Do Count

In dieting we hear a lot about calories. One popular diet book some years ago was titled "Calories Don't Count." The only problem with this title is that calories do indeed count. Whether you count 'em or not, it's calorie balance (intake vs. output) that determines weight.

Think of calories as fuel, the fuel that is used to keep you alive, alert and moving, says a new pamphlet from the American Medical Association. If you take in more fuel each day than your body can use, the excess is stored.

Most people leading moderately active lives need about 15 calories per pound to maintain their weight. So if you want to stay, say, at 150 pounds, you can eat foods containing no more than 2,250 calories each day.

But if you're well above your ideal weight, you'll have to cut

back on your calorie intake and use more of the stored fuel. There are approximately 3,500 calories in each pound of stored fat. So to lose one pound a week, consume 500 fewer calories each day. Or if you want to lose two pounds each week cut down by 1,000 calories each day. It usually is unwise to lose more than two pounds a week.

If your motive is to lose weight quickly so that you can get back to thick milk-shakes, 12-ounce steaks and high-calorie bedtime snacks, you are probably going to have lifelong weight problems. A slow and sensible weight loss program can offer conditioning and training toward a better way of eating to keep the weight down the rest of your life.

If you are obese (more than 20 per cent over the desired weight for your height and build) or have had a weight problem for many years, see your family doctor before launching any do-it-yourself diet. Some heavy people have unsuspected illness and it would be foolhardy to complicate any problems by postponing treatment or following an inappropriate diet.



April, 1979

Frank Chappell  
Science News Editor  
AMA

Unlock arthritis pain  
and inflammation with  
the right combination!

# Ascriptin<sup>®</sup> A/D

Arthritic Doses



## Aspirin 325 mg.

Still the rheumatologist's  
anti-inflammatory analgesic drug  
of choice for the control of arthritis.

## Maalox<sup>®</sup> 300 mg.

Still the gastroenterologist's antacid  
of choice, providing dependable gastric  
protection at optimum dosage levels.

## Ascriptin<sup>®</sup> A/D

Now a better approach for salicylate control  
of arthritis with less gastric irritation  
(as illustrated by endoscopy\*).

\* Data on file, William H. Rorer Medical Department.



**WILLIAM H. RORER, INC.**  
Fort Washington, Pa. 19034



In pediatric infections

# Septra<sup>®</sup>

Each teaspoonful (5 ml) contains:  
40 mg trimethoprim and 200 mg sulfamethoxazole

## Suspension B.I.D.

Acute  
Otitis  
Media



where  
the action is.

# In acute otitis media

Septra Suspension provides effective antibacterial action against susceptible strains of H influenzae and S pneumoniae (D pneumoniae), the pathogens most likely to cause acute otitis media in children.

Septra Suspension is useful in many patients, but especially in those with penicillin allergy or with infections caused by ampicillin-resistant H influenzae. Limited clinical data are presently available on the effectiveness of treatment of acute otitis media with Septra when the infection is due to H influenzae resistant to ampicillin. However, in vitro data is highly favorable; when over 200 strains of ampicillin-resistant H influenzae were tested, all proved susceptible to TMP/SMX.\*

And unlike most other antibacterials for the treatment of acute otitis media, Septra Suspension is administered on a convenient b.i.d. dosage schedule. The cherry-flavored suspension is well accepted by children.



# In recurrent urinary tract infections

Septra Suspension provides effective antibacterial action in urine and blood against susceptible strains of E coli, Klebsiella-Enterobacter and Proteus. Whether the infection centers in the kidneys or bladder, Septra Suspension maintains effective levels at the site of the infection with just two doses a day.

Adequate fluid intake should be maintained and frequent urinalyses with careful microscopic examination performed during Septra therapy. Septra is contraindicated in infants under two months of age.

\*In vitro data do not necessarily correlate with clinical results. Data on file, Burroughs Wellcome Co.  
NOTE: Septra should not be used in the treatment of streptococcal pharyngitis.

*Please see prescribing information on next page.*



Wellcome

**Burroughs Wellcome Co.**  
Research Triangle Park  
North Carolina 27709



# Septra® Suspension B.I.D.

Each teaspoonful (5 ml) contains: 40 mg trimethoprim and 200 mg sulfamethoxazole

# Septra® DS B.I.D.

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Septra® DS Tablets Double Strength

Septra® Tablets

Septra® Suspension

### INDICATIONS AND USAGE:

**URINARY TRACT INFECTIONS:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

**NOTE:** Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

**ACUTE OTITIS MEDIA:** For the treatment of acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to *Haemophilus influenzae* resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.

**SHIGELLOSIS:** For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

**PNEUMOCYSTIS CARINII PNEUMONITIS:** For the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

**CONTRAINDICATIONS:** Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

**WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.**

Clinical studies have documented that patients with Group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

**PRECAUTIONS:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

**ADVERSE REACTIONS:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood Dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic Reactions:** Erythema multiforme, Stevens-Johnson

syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal Reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **C.N.S. Reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous Reactions:** Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L. E. phenomenon have occurred.

Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

**DOSAGE AND ADMINISTRATION:** Not recommended for use in infants less than two months of age.

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:**

**Adults:** The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

**Children:** The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose —every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 ( 5 ml)	½
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1½
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

### PNEUMOCYSTIS CARINII PNEUMONITIS:

The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose —every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 ( 5 ml)	½
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1½
70	32	4 (20 ml)	2 (or 1 DS tablet)

**HOW SUPPLIED:** TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

**ORAL SUSPENSION,** containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709



ROCHE

# For recurrent attacks of urinary tract infection in women

## Bactrim<sup>TM</sup> DS Double Strength Tablets

Each tablet contains 160 mg trimethoprim and 800 mg sulfamethoxazole.

### Just one tablet b.i.d. for 10 to 14 days



- Action at urinary/vaginal/lower bowel sites helps eliminate reservoirs of infecting organisms
- Distinctive antibacterial action plus wide spectrum helps eradicate recurrent UTI
- Low incidence of bacterial resistance in community practice

- Convenient b.i.d. dosage provides day-and-night antibacterial control
- Contraindicated during pregnancy and the nursing period. During therapy, maintain adequate fluid intake; perform CBC's and urinalyses with microscopic examination.

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications and Usage:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination. Note: The increasing frequency of resistant organisms limits the usefulness of all antibacterials, especially in these urinary tract infections.

**Also for the treatment of documented *Pneumocystis carinii* pneumonitis.** To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

The recommended quantitative disc susceptibility method (Federal Register, 37:20527-20529, 1972) may be used to estimate bacterial susceptibility to Bactrim. A laboratory report of "Susceptible to trimethoprim-sulfamethoxazole" indicates an infection likely to respond to Bactrim therapy. If infection is confined to the urine, "Intermediate susceptibility" also indicates a likely response. "Resistant" indicates that response is unlikely.

**Contraindications:** Hypersensitivity to trimethoprim or sulfonamides; pregnancy; nursing mothers; infants less than two months of age.

**Warnings:** Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been associated with sulfonamides. Experience with trimethoprim is much more limited but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides. Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBC's are recommended; therapy should be discontinued if a significantly reduced count of any formed blood element is noted.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In patients with glucose-6-phosphate dehydrogenase deficiency, hemolysis, frequently dose-related, may occur. During therapy, maintain adequate fluid intake and perform frequent urinalyses, with careful microscopic examination, and renal function tests, particularly where there is impaired renal function.

**Adverse Reactions:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Bactrim. **Blood dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprolthrombinemia and methemoglobinemia. **Allergic reactions:** Erythema multiforme, Stevens-Johnson syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **CNS reactions:** Headache,

peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous reactions:** Drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon. Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia in patients; cross-sensitivity with these agents may exist. In rats, long-term therapy with sulfonamides has produced thyroid malignancies.

**Dosage:** Not recommended for infants less than two months of age.

**Urinary Tract Infections:** Usual adult dosage—1 DS tablet (double strength), 2 tablets (single strength) or 4 teasp. (20 ml) b.i.d. for 10-14 days.

Recommended dosage for children—8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, in two divided doses for 10 days. A guide follows:

Children two months of age or older

Weight		Dose—every 12 hours	
lbs	kgs	Teaspoonfuls	Tablets
20	9	1 teasp. (5 ml)	½ tablet
40	18	2 teasp. (10 ml)	1 tablet
60	27	3 teasp. (15 ml)	1½ tablets
80	36	4 teasp. (20 ml)	2 tablets or 1 DS tablet

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual standard regimen
15-30	½ the usual regimen
Below 15	Use not recommended

***Pneumocystis carinii* pneumonitis:** Recommended dosage: 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours in equal doses every 6 hours for 14 days. See complete product information for suggested children's dosage table.

**Supplied:** Double Strength (DS) tablets, each containing 160 mg trimethoprim and 800 mg sulfamethoxazole, bottles of 100, Tel-E-Dose® packages of 100 Tablets, each containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 100 and 500; Tel-E-Dose® packages of 100; Prescription Paks of 40, available singly and in trays of 10. Oral suspension, containing in each teaspoonful (5 ml) the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole, fruit-licorice flavored—bottles of 16 oz (1 pint).

ROCHE

Roche Laboratories  
Division of Hoffmann-La Roche Inc.  
Nutley, New Jersey 07110

Please see back cover.

Her next attack of cystitis may require

# the Bactrim<sup>™</sup> 3-system counterattack



ROCHE

Bactrim has shown high clinical effectiveness in recurrent cystitis as a result of its wide spectrum and distinctive antimicrobial action in the urinary, vaginal and lower intestinal tracts.

The probability of recurrent urinary tract infection appears to be enhanced by the establishment of large numbers of *E. coli* or other urinary pathogens on the vaginal introitus. The trimethoprim component of

Bactrim diffuses into vaginal fluid in effective concentrations, thus combating migration of pathogens into the urethra.

Studies have shown that Bactrim acts against *Enterobacteriaceae* in the bowel without the emergence of resistant organisms. Thus, Bactrim reduces the risk of introital colonization by fecal uropathogens. It has no significant effect on other normal, necessary intestinal flora.

## Bactrim fights uropathogens in the urinary tract/vaginal tract/lower intestinal tract

Please see reverse side for summary of product information.





# BOLETIN

ASOCIACION MEDICA DE PUERTORICO

C O N T E N I D O:

NEW ADVANCES IN THE IMMUNODIAGNOSIS OF PARASITIC INFECTIONS

I. THE ENZYME-LINKED IMMUNOSORBENT ASSAY

KIDNEY STONES: A MEDICAL APPROACH

BRIEF COMMUNICATION: INSIDIOUS METHYL ALCOHOL POISONING

EDITORIAL: USO EXPERIMENTAL Y CLINICO DE INJERTOS  
VASCULARES DE POLITETRAFLOROETILENO

ABSTRACTOS: REGIONAL MEETING AMERICAN COLLEGE  
OF PHYSICIANS — OCT. 19-20/79

NOTICIAS

MEDI-QUIZ

INDICE ..... PAGINA 366



# PERFORMANCE. PROVEN EFFECTIVENESS WITHIN A WIDE SAFETY MARGIN.



While Roche Laboratories already knows more about the performance of Librium than anyone else, we keep on learning every day.

For example, the highly favorable benefits-to-risk ratio of Librium is a well-documented matter of record.

And, of course, the specific calming action of Librium has been demonstrated in millions of patients around the world. In a large number of these patients, Librium was used concomitantly with other primary medications.

Proven performance within a wide safety margin. Basically, that's what Librium is all about.

## LIBRIUM® chlordiazepoxide HCl/Roche THE ANXIETY-SPECIFIC

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Relief of anxiety and tension occurring alone or accompanying various disease states. Efficacy beyond four months not established by systematic clinical studies. Periodic reassessment of therapy recommended.

**Contraindications:** Patients with known hypersensitivity to the drug.

**Warnings:** Warn patients that mental and/or physical abilities required for tasks such as driving or operating machinery may be impaired, as may be mental alertness in children, and that concomitant use with alcohol or CNS depressants may have an additive effect. Though physical and psychological dependence have rarely been reported on recommended doses, use caution in administering to addiction-prone individuals or those who might increase dosage; withdrawal symptoms (including convulsions), following discontinuation of the drug and similar to those seen with barbiturates, have been reported.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malforma-

tions as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** In the elderly and debilitated, and in children over six, limit to smallest effective dosage (initially 10 mg or less per day) to preclude ataxia or oversedation, increasing gradually as needed and tolerated. Not recommended in children under six. Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider individual pharmacologic effects, particularly in use of potentiating drugs such as MAO inhibitors and phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions (e.g., excitement, stimulation and acute rage) have been reported in psychiatric patients and hyperactive aggressive children. Employ usual precautions in treatment of anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation have been reported very rarely in patients receiving the drug and oral anticoagulants; causal relationship has not been established clinically.

**Adverse Reactions:** Drowsiness, ataxia and confusion may occur, especially in the elderly and debilitated. These are reversible in most instances by proper dosage adjustment, but are also occasionally observed at the lower dosage ranges. In a few instances syncope has been reported. Also encountered are isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent and generally controlled with dosage reduction; changes in EEG patterns (low-voltage fast activity) may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice and hepatic dysfunction have been reported occasionally, making periodic blood counts and liver function tests advisable during protracted therapy.

**Supplied:** Librium® Capsules containing 5 mg, 10 mg or 25 mg chlordiazepoxide HCl. Libritabs® Tablets containing 5 mg, 10 mg or 25 mg chlordiazepoxide.



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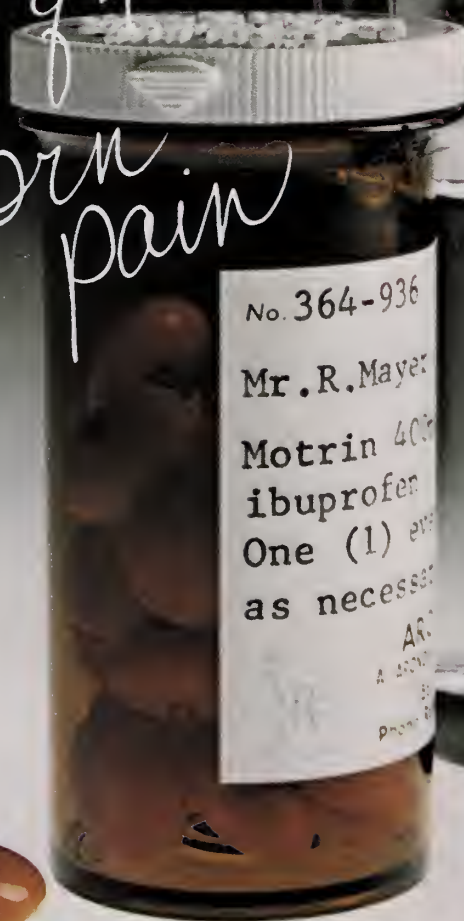
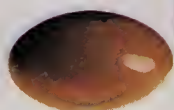
The Upjohn Company  
announces  
a new  
indication for  
Motrin<sup>®</sup>  
(ibuprofen)



A well-tolerated, nonnarcotic prescription for pain

Motrin tablets  
400 mg

Sig T q 4-6 h  
prn  
pain





# Motrin now proved an effective analgesic for mild to moderate pain

Motrin 400 mg provided greater relief of pain than did propoxyphene 65 mg in controlled clinical pain studies.

Time after drug administration (hour)		.5	1	2	3	4
Mean relief-of-pain scores* (No. patients reporting)	Motrin 400 mg ibuprofen	.89 (108)	1.25 (108)	1.36 (108)	1.28 (107)	1.19 (106)
	Darvon 65 mg propoxyphene	.66 (100)	.99 (99)	1.13 (96)	.99 (96)	.80 (96)
Statistical significance		p<0.02	p<0.01	p<0.05	p<0.02	p<0.002

\*0 = No relief    1 = Partial relief    2 = Complete relief

Data on file at The Upjohn Company

Motrin demonstrated statistically significant greater relief of pain than did Darvon at all time intervals.

**Motrin** 400<sup>TABLETS</sup>mg  
ibuprofen, Upjohn

- Not a narcotic • Not addictive • Not habit forming
- Rapid analgesic action • Indicated in acute and chronic pain
- Well tolerated. The most common side effect with Motrin is mild gastrointestinal disturbance.

Please turn the page for a brief summary of prescribing information.

# Motrin<sup>®</sup> (ibuprofen)

## now proved an effective analgesic for mild to moderate pain

**Motrin<sup>®</sup> Tablets** (ibuprofen, Upjohn)

**Indications and Usage:** Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management. Safety and efficacy have not been established in Functional Class IV rheumatoid arthritis.

Relief of mild to moderate pain.

**Contraindications:** Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

**Warnings:** Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

**Precautions:** Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.

**Drug interactions.** Aspirin used concomitantly may decrease Motrin blood levels. **Coumarin:** Bleeding has been reported in patients taking Motrin and coumarin.

**Pregnancy and nursing mothers:** Motrin should not be taken during pregnancy or by nursing mothers.

### Adverse Reactions

#### Incidence greater than 1%

**Gastrointestinal:** The most frequent type of adverse reaction occurring with Motrin is gastrointestinal (4% to 16%). This includes nausea\*, epigastric pain\*, heartburn\*, diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness\*, headache, nervousness. **Dermatologic:** Rash\* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

\*Incidence 3% to 9%.

#### Incidence less than 1 in 100

**Gastrointestinal:** Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

#### Causal relationship unknown

**Gastrointestinal:** Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

**Overdosage:** In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine, so alkaline diuresis may be beneficial.

**Dosage and Administration:** Rheumatoid and osteoarthritis, including flares of chronic disease: Suggested dosage is 300, 400 or 600 mg t.i.d. or q.i.d.

Mild to moderate pain: 400 mg every 4 to 6 hours as necessary for relief of pain.

Do not exceed 2400 mg per day.

**Caution:** Federal law prohibits dispensing without prescription.

For additional product information, see your Upjohn representative or consult the package insert.

**Upjohn** THE UPJOHN COMPANY  
Kalamazoo, Michigan 49001 USA

MED B-4-S

**ALDORIL<sup>®</sup>**  
containing methyldopa and hydrochlorothiazide

#### TABLETS

### ALDORIL<sup>®</sup>-25

containing 250 mg ALDOMET<sup>®</sup> (Methyldopa, MSD) and 25 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

#### TABLETS

### ALDORIL<sup>®</sup>-15

containing 250 mg ALDDMET<sup>®</sup> (Methyldopa, MSD) and 15 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

#### TABLETS

### ALDORIL<sup>®</sup> D30

containing 500 mg ALDOMET<sup>®</sup> (Methyldopa, MSD) and 30 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

#### TABLETS

### ALDORIL<sup>®</sup> D50

containing 500 mg ALDDMET<sup>®</sup> (Methyldopa, MSD) and 50 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

Merck Sharp & Dohme, Division of  
Merck & Co., Inc., West Point, PA 19486

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Fundado en 1903

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\* New Advances in the Immunodiagnosis of Parasitic Infections - I. The Enzyme-Linked Immunosorbent Assay ..... 366  
*George V. Hillyer, Ph D and Irving G. Kagan, Ph D*

Este es el primero de una serie de artículos sobre nuevos adelantos en el diagnóstico inmunológico de infecciones parasíticas. El autor resume la literatura sobre el uso de ELISA (enzyme-linked immunosorbent assay), y presenta las aplicaciones clínicas de esta técnica.

\* Kidney Stones: A Medical Approach ..... 378  
*Laura E. Lespier-Dexter, MD*

Nephrolithiasis is a very common disorder in Puerto Rico. Dra. Lespier presents important pathophysiological, diagnostic and therapeutic aspects on this important medical problem. Her approach to the diagnostic evaluation of these patients include determination of serum Co, P<sub>2</sub> and uric acid. Determination of urinary cyclic AMP is generally not required for management and should be reserved for selected cases. The author emphasizes the beneficial effects of thiazides alone or in combination with allopurinol in the prevention of recurrent stones. The article should be of great interest to all of our readers.

\* Insidious Methyl Alcohol Poisoning ..... 384  
*Sidney Kaye, MSc, PhD*

On this brief communication Dr. Kaye presents useful information for the rapid diagnosis, identification and treatment of methyl alcohol poisoning.

Several years ago, there was an outbreak of food poisoning in Ponce. This resulted in at least seven deaths according to the author. Upon examination of the cadavers, it was discovered that the outbreak was due to methanol poisoning. The hints provided in this article should make us aware of the clinical presentation of this condition.

\* Editorial: Uso Experimental y Clínico de Injertos Vasculares de Politetrafluoroetileno ..... 388  
*E. A. Santiago Delpín, MD*

\* Abstractos: Regional Meeting of American College of Physicians October 19-20/79 ..... 390

\* Noticias ..... 406

\* Medi-Quiz ..... 405

# NEW ADVANCES IN THE IMMUNODIAGNOSIS OF PARASITIC INFECTIONS. I. THE ENZYME-LINKED IMMUNOSORBENT ASSAY

George V. Hillyer, PhD and Irving G. Kagan, PhD

**Summary:** This is the first of a series of reviews related to new advances in the immunodiagnosis of parasitic infections. A sensitive quantitative technique known as the enzyme-linked immunosorbent assay (ELISA) has been adapted for the serodiagnosis of infections with a wide variety of animal parasites. The available literature on its application is reviewed here.

**Resumen:** En el primero de una serie de ensayos sobre nuevos adelantos en el inmunodiagnóstico de infecciones parasíticas se resume la literatura sobre el uso de una técnica inmunoenzimológica sensitiva y cuantitativa conocida como ELISA (enzyme-linked immunosorbent assay).

## Introduction

The enzyme-linked immunosorbent assay (ELISA) described by Engvall and Perlmann (1971) has received considerable attention with respect to its use in the diagnosis of parasitic and other diseases. During the past 5 years the literature describing the ELISA has blossomed and numerous reviews and at least one technical manual have been published (Table I).

Enzyme immunoassays combine the advantages of immunofluorescence (IIF) and radioimmunoassay (RIA) and have additional advantages in that the enzyme labelled reagents are inexpensive to prepare, are highly stable, having a long shelf life, and yield assays approaching the sensitivity of RIA.

This review covers the use of enzyme immunoassays for the diagnosis of parasitic infections. In this test soluble antigens or antibody are linked to an insoluble solid phase in such a manner that immunologic reactivity is retained. The method, summarized in the elegant acronym "ELISA" was pioneered by Engvall and colleagues (1971) and by Van Weemen and Schurs (1971, 1972). The method was originally described using polystyrene tubes (macro-ELISA) and was quantitated spectrophotometrically. A modification utilizing microtiter plates (micro-ELISA) required smaller amounts of reactants (Voller, et al, 1974). Both the macro- and micro-ELISAs may be read visually by end point titration. Equipment to read microtitration ELISA plates spectrophotometrically are now available commercially.

The literature on use of the ELISA for the diagnosis of parasitic infections is summarized below by groups.

## Protozoa

The ELISA test for malaria was evaluated by Voller et al (1974) and Gentilini and Richard Lenable (1975). Voller, et al (1974) developed

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*From the Laboratory of Parasite Immunology, Department of Biology, University of Puerto Rico, Río Piedras, Puerto Rico, 00931 and the Parasitology Division, Center for Disease Control, Atlanta, Georgia 30333.*

TABLE I

Summary of Selected Reviews on the Use of the Enzyme-  
Linked Immunosorbent Assay for Serodiagnosis

References	Subject
<i>Capron et al, 1975</i>	<i>Application to various parasitic infections</i>
<i>Bout et al, 1975 (a, b)</i>	<i>Application to various parasitic infections</i>
<i>Bout et al, 1976 (a, b)</i>	<i>Correlation with other serological techniques</i>
<i>Scharpe et al, 1976</i>	<i>Review of enzyme-immunoassays</i>
<i>Voller et al, 1976 (a, b)</i>	<i>Application to various parasitic infections</i>
<i>Wisdom, 1976</i>	<i>Review of enzyme-immunoassays</i>
<i>W. H. O., 1976</i>	<i>Detailed description of method and applications</i>
<i>Bulloch and Walls, 1977</i>	<i>Evaluation of parameters</i>
<i>Ruitenbergh et al, 1977</i>	<i>Application to various parasitic infections</i>
<i>Voller et al, 1977a</i>	<i>Comparison with radioimmunoassay</i>
<i>Voller, 1977b</i>	<i>Commercial review-with bibliography</i>
<i>Walls and Palmer, 1978</i>	<i>Technical Manual</i>
<i>Nakamura et al, 1979</i>	<i>5 reports on how to do it</i>

\* - For complete citations, see References

a micro-ELISA and showed its applicability in a small seroepidemiological study of individuals from Colombia. Using *P. falciparum* antigen obtained from the blood of *Aotus trivirgatus* monkeys he found higher titers of antibody in individuals from an endemic area for malaria than in those where an effective malaria eradication program had been implemented. (Voller, et al, 1975). Utilizing a heterologous antigen from *P. knowlesi* the serum of individuals with *P. vivax* or *P. falciparum* from Iran were tested (Voller et al, 1975). A wide range of reactivity reflecting the low malarial endemicity in Iran was reported and sera from a malarious area of Tanzania gave higher va-

lues than sera from European controls. In addition, two New Guinean populations were compared: one from Marakawa at an altitude of 2,000 meters where malaria transmission is absent with low ELISA values; the other group from Usino in the lowlands where malaria is endemic with high ELISA values. These values increased with age which were interpreted in terms of malaria transmission intensity (Voller, et al 1976a). In comparing ELISA and isotopic assays with sera from the New Guinean populations, as well as European negative controls, they found both assays to be sensitive and reproducible and gave comparable results (Voller, et al, 1977).



TABLE II  
Use of the Enzyme-Linked Immunosorbent Assay for the Serodiagnosis of  
Infections with Parasitic Protozoa

<i>Parasite Infection</i>	<i>Detection</i>	<i>References</i>
<i>Plasmodium falciparum</i>	<i>Antibodies in man</i>	<i>Voller et al, 1974</i> <i>Gentilini and Richard-Lenoble, D., 1975</i> <i>Voller et al, 1975</i> <i>Voller et al, 1976a</i> <i>Voller et al, 1977</i>
<i>P. vivax</i>	<i>Antibodies in man</i>	<i>Gentilini and Richard-Lenoble, D., 1975</i> <i>Voller et al, 1975</i>
<i>Trypanosoma gambiense</i>	<i>Antibodies in man</i>	<i>Voller et al 1976a</i>
African trypanosomiasis	<i>Antibodies in rabbits and man</i>	<i>Ruitenbergh et al, 1977</i> <i>Voller et al, 1977</i>
<i>T. vivax</i>	<i>Antibodies in cattle</i>	<i>Voller et al, 1975</i>
<i>T. cruzi</i>	<i>Antibodies in man</i>	<i>Voller et al, 1975</i> <i>Voller et al, 1976a</i> <i>Voller et al, 1977</i>
<i>Leishmania donovani</i>	<i>Antibodies in man</i>	<i>Edrissian and Darabian, 1978</i> <i>Edrissian and Darabian, 1979</i>
<i>L. infantum</i>	<i>Antibodies in man and dog</i>	<i>Hommel et al, 1978</i>
<i>L. tropica</i>	<i>Antibodies in man</i>	<i>Edrissian and Darabian, 1978</i> <i>Edrissian and Darabian, 1979</i>
<i>Toxoplasma gondii</i>	<i>Antibodies in man</i>	<i>Capron et al, 1975</i> <i>Bout et al, 1975</i> <i>Bout et al, 1976</i> <i>Voller et al, 1976a</i> <i>Voller et al, 1976c</i> <i>Walls et al, 1977</i> <i>Camargo et al, 1978</i>
<i>Babesia divergens</i>	<i>Antibodies in cattle</i>	<i>Voller et al, 1976a</i>
<i>Entamoeba histolytica</i>	<i>Antibodies in man</i>	<i>Bos et al, 1975</i> <i>Voller et al, 1976a</i> <i>Voller, 1977</i> <i>Felgner, 1977</i>

Approximately 90 percent of slide proven cases of african trypanosomiasis in man had sera with positive ELISA values when *T. brucei* was used as antigen (Voller, et al 1976a). The specificity of the test was excellent. None of the control sera from Africans free of trypanosome infections but exposed to malaria and/or schistosomiasis had positive values. Cross-reactivity was observed with sera from patients with Chagas' disease (Voller, et al, 1977). Ruitenbergh, et al (1977) detected homologous and heterologous anti-trypanosome antibodies in rabbits with *T. brucei* or *T. rhodesiense* 4-8 weeks post-infection and found the sensitivity of the ELISA comparable to IIF. The test was also useful for the detection of individuals with proven sleeping sickness from Congo, Brazzaville. Cross-reactions were observed with the serum from a patient with leishmaniasis from Surinam, but none were observed with patients with malaria, toxoplasmosis, schistosomiasis or echinococcosis. Voller, et al (1976a) found that a calf infected with *T. vivax* had detectable antibodies two-and-one-half weeks after infection and were still at high levels six months later. In studies of Brazilians with Chagas' disease Voller et al (1975, 1976a, 1977) found the ELISA to be an adequate technique for immunodiagnosis and correlated well with immunofluorescence and isotopic assays. The sera of patients with African sleeping sickness cross-reacted with the *T. cruzi* antigen.

Edrissian and Darabian (1978, 1979) found IIF more specific than ELISA for the diagnosis of cutaneous leishmaniasis, but neither were as satisfactory as examinations of biopsy by microscopy. Both serological methods were adequate for the diagnosis of visceral leishmaniasis when promastigote forms of *L. donovani* were used as antigen. Hommel et al (1978) found the ELISA highly sensitive and specific for the diagnosis of human and canine visceral leishmaniasis.

Numerous articles have been published utilizing the ELISA for the serodiagnosis of toxoplasmosis. The early reports by Capron and collaborators (Capron, et al, 1975; Bout, et al, 1975, 1976) and of Voller et al (1976a, 1976c) demonstrated reasonable correlations between the ELISA, indirect hemagglutination (IHA), direct agglutination, and dye tests. Walls, et al (1977), utilizing solubilized taquizoites found the test 98 percent specific, highly reproducible, and obtained results equivalent to the IIF test. Camargo et al (1978) performed the ELISA test utilizing anti IgG and anti IgM antibodies and considered it an acceptable substitute for IIF.

Cattle infected with *Babesia divergens* had detectable parasites in the blood one week prior to the detection of high ELISA titers. Additional work will be required to study the suitability of this test to detect active infections since titers continued to rise while parasitemia dropped (Voller, et al, 1976a).

Bos et al (1975) and Voller et al (1976a) found higher ELISA titers in patients with hepatic as compared to intestinal amebiasis or normal controls. Furthermore, ELISA and  $^{125}\text{I}$  assays were equally effective in detecting patients with invasive amebiasis when *E. histolytica* was used as antigen. Cross-reactivity was observed with sera from patients with African sleeping sickness. Felgner (1977) introduced a stick-ELISA test using polystyrene sticks as the solid phase.

This summary indicates that the ELISA has been extensively evaluated for the serodiagnosis of protozoan infections. In the case of toxoplasmosis a commercial reagent is available (Worthington Diagnostics, a Division of Millipore Corporation).

### Trematodes

Numerous articles have appeared in the

TABLE III

Use of the Enzyme-Linked Immunosorbent Assay for the Serodiagnosis of  
Infections with Trematodes

<i>Parasite Infection</i>	<i>Detection</i>	<i>References</i>
<i>Schistosoma mansoni</i>	<i>Antibodies in man, mice and monkeys</i>	<i>Capron et al, 1975</i>
		<i>Huldt et al, 1975</i>
		<i>Bout et al, 1976</i>
		<i>Schinsky et al, 1976</i>
		<i>Voller et al, 1976</i>
		<i>Ahmed et al, 1977</i>
		<i>Deelder et al, 1977</i>
		<i>Pinon and Dropsy, 1977a, b</i>
		<i>Polderman and Deelder, 1977</i>
		<i>Voller et al, 1977</i>
		<i>McLaren et al, 1978</i>
		<i>Pinon et al, 1978</i>
	<i>Anti-DNA antibodies</i>	<i>Stek, Jr., 1978</i>
		<i>Kelsoe and Weller, 1978</i>
		<i>Hillyer and Gómez de Ríos, 1979</i>
		<i>Lunde et al, 1979</i>
		<i>Maddison et al, 1979a, b</i>
		<i>Hillyer et al, 1979</i>
		<i>Hillyer and Rossy, 1978</i>
		<i>Hillyer and Rossy, 1980</i>
	<i>Antigens in man</i>	<i>Voller et al, 1976</i>
		<i>Stek, Jr., 1978</i>
<i>S. haematobium</i>	<i>IgG antibodies in man</i>	<i>Schinsky et al, 1978</i>
<i>S. japonicum</i>	<i>Antibodies in mice</i>	<i>Hillyer and Bruce, 1980</i>
<i>S. mekongi</i>	<i>Antibodies in mice</i>	<i>Hillyer and Bruce, 1980</i>
<i>Fasciola hepatica</i>	<i>Antibodies in man</i>	<i>Carlier et al, 1979</i>
	<i>Antibodies in cattle</i>	<i>Grelch and Horchner, 1977</i>
		<i>Burden and Hammet, 1978</i>
	<i>Antibodies in rats and rabbits</i>	<i>Hillyer, 1978</i>
		<i>Hillyer and Santiago de Weil, 1979</i>



literature applying the ELISA for the detection of antibodies and antigens in infections with schistosomes. Capron, et al (1975) and Bout et al (1976) used a crude extract from adult worms and found that the ELISA could readily differentiate persons with infections of *S. mansoni* over normal controls or persons with other parasitic infections. Huldt, et al (1975) found that a purified egg antigen was superior to a crude adult worm antigen in distinguishing cases of schistosomiasis from Zaire and Sudan versus sera from Swedish controls. Schinsky, et al (1976) used a freeze-thaw antigen of adult worms of *S. mansoni* and found the ELISA and RIA considerably more sensitive than IHA and HF, Voller, et al (1977) also found ELISA and radioimmunoassay to be equally sensitive in detecting individuals with antibodies to egg antigens of *S. mansoni* and observed no cross-reactions with sera from patients with malaria or Chagas' disease. Ahmed et al (1977) found the enzyme conjugate more sensitive than the fluorescein conjugate. McLaren, et al (1978), Maddison, et al (1979, a,b), and Hillyer and Gómez de Ríos (1979) demonstrated antibodies to egg antigens in chimpanzees, rhesus monkeys and mice with schistosomiasis mansoni. McLaren, et al (1978) found the ELISA test using a soluble egg antigen preparation (SEA) as sensitive as IIF and complement fixation (CF) using adult worms as antigen, but stated that the ELISA was more specific. Hillyer and Gómez de Ríos (1979) found that although the ELISA was useful in detecting antibodies to SEA in individuals with infections of *S. mansoni* as compared to uninfected controls, extensive cross-reactivity was observed with the sera of humans with fascioliasis, trichinosis, cysticercosis and echinococcosis. In addition, they observed that end-point titrations were superior to one-point dilution when performing the micro-ELISA. Deelder, et al (1977) compared the ELISA and the defined antigen substrate

spheres (DASS) systems using extracts of adult worms with IIF utilizing cryocut sections of worms and found the first to be at least as specific and sensitive as, and with considerable advantages over, IIF. However, in a field study with the three methods and, in addition IHA, Polderman and Deelder (1977) found that all four serologic tests lacked in sensitivity and specificity. With all four techniques a decline in titers with increasing age was observed, rather independent of the presence or absence of *S. mansoni* eggs in the corresponding stool samples. However, since three different types of stool examinations were used in this study, all with different sensitivities, these findings must be interpreted with caution. Stek (1978) used four different antigen preparations of *S. mansoni* in a micro-ELISA and could detect anti-schistosomosome IgG in the serum of humans with schistosomiasis mansoni and haematobia. He also demonstrated a significant difference between the acute and chronic patients when anti-schistosomosome IgM antibody was measured. Hillyer et al (1979) compared ELISA, RIA, Ouchterlony immunodiffusion, and the circumoval precipitin (COP) test using eggs or egg antigens for the serodiagnosis of human schistosomiasis mansoni. Both RIA with pure MSA<sub>1</sub> as antigen and the COP test had a diagnostic sensitivity of 95 percent and detected 100 percent of the individuals excreting 10 or more eggs per gram feces. The ELISA had a specificity of 92 percent but sensitivity of 75 percent. Hillyer and Bruce (1980) used the ELISA to detect antibodies in murine schistosomiasis japonica and mekongi, the latter a new schistosomosome infection of man. Lunde et al (1979) suggested that the sera from patients with acute schistosomiasis reacted more positively to cercarial antigen and the sera from patients with chronic schistosomiasis reacted more positively with adult worm antigens. Hillyer and Rossy (1978, 1980) demonstrated anti-DNA antibodies in mice

TABLE IV  
Use of the Enzyme-Linked Immunosorbent Assay for the Serodiagnosis of  
Infections with Cestodes or Nematodes

<i>Parasite Infection</i>	<i>Detection</i>	<i>References</i>
<i>Cestodes</i>		
<i>Echinococcus granulosus</i>	<i>Antibodies in man</i>	<i>Bout et al, 1975</i> <i>Capron et al, 1975</i> <i>Farag et al, 1975</i> <i>Voller et al, 1975</i> <i>Bout et al, 1976</i> <i>Pinon and Dropsy 1977a, b</i> <i>Pinon et al, 1978</i> <i>Pinon et al, 1979</i>
<i>Nematodes</i>		
<i>Trichinella spiralis</i>	<i>Antibodies in swine</i>	<i>Ruitenberget al, 1974 a, b</i> <i>Ljungstrom et al, 1974</i> <i>Ruitenberget al, 1975 a, b</i> <i>Ruitenberget al, 1976 a, b</i> <i>Ruitenberget al, 1977</i> <i>Saunders et al, 1977</i>
	<i>Antibodies in man</i>	<i>Engvall and Ljunstrom, 1975</i>
	<i>Mechanization for large scale screening</i>	<i>Ruitenberget al, 1977</i>
<i>Toxocara canis</i>	<i>Antibodies in monkeys</i>	<i>Ruitenberget al, 1977</i> <i>Schantz et al, 1978</i>
	<i>Antibodies in man</i>	<i>Cypess et al, 1977</i> <i>Glickman et al, 1978</i> <i>Schantz et al, 1979</i> <i>Glickman et al, 1979</i>
<i>Onchocerca volvulus</i>	<i>Antibodies in man</i>	<i>Bartlett et al, 1976</i>

infected with *S. mansoni* by 6 weeks post-exposure which persisted through the 18 weeks tested. A drop in titers at 7, 9, and 11 weeks suggests the presence of circulating DNA and/or immune complexes.

Voller et al (1976a) showed the presence of circulating egg antigen in the serum of humans with *S. mansoni*, although the results were not clear-cut. Kelsoe and Weller coupled a polysaccharide schistosome antigen to poly-L-lysine-coated wells and found the test useful for the serodiagnosis of human schistosomiasis mansoni. Stek (1978) found no false positive results when detecting circulating antigen by micro-ELISA. Schinsky, et al (1978) demonstrated specific IgG antibodies in humans with schistosomiasis haematobia. Pinon et al (1978) combined immunoelectroimmunodiffusion with enzyme-linked antibodies (see Cestodes) in a technique called ELIEDA and found it useful for the detection of antibodies in human and experimental schistosomiasis.

Grelch and Horchner (1977) compared the ELISA and IIF for the serodiagnosis of bovine fascioliasis. Burden and Hammet (1978) also used the ELISA to detect bovine fascioliasis and, in addition, found no cross-reactivity of the *F. hepatica* antigen when testing the serum of calves infected with *Ostertagia ostertagi*.

Application of the ELISA for the detection of antibodies to extracts of adult worms partially purified by Sephacryl S-200 chromatography in rats and rabbits with fascioliasis has been demonstrated by Hillyer (1978) and Hillyer and Santiago de Weil (1979). Titers rose by 4 (rats) or 6 (rabbits) weeks of infection and remained high for at least 28 weeks. These titers dropped rapidly in animals successfully treated with a fasciolicidal drug.

In summary, the ELISA has been used extensively to detect both antigen and antibody in natural and experimental infections with schistosomes but the full potential for

the technique awaits the use of purified antigens.

### Cestodes

The ELISA has been valuable in the immunodiagnosis of human hydatid disease. Bout et al (1975, 1976), Capron, et al (1975), and Farag, et al (1975) used whole hydatid fluid or purified F5 antigen and found no overlap between normal individuals and hydatid patients. The extinction values obtained by spectrophotometry of the ELISA were in agreement with the number of bands found immunoelectrophoresis by (IEP) and by IIF titers. Voller, et al (1975) also found excellent agreement between the ELISA values and IIF titers in serum from Brazilians with hydatid disease.

Pinon and collaborators (1977, 1979) improved the sensitivity of immunoelectrodiffusion (IED) by treating the precipitated immune complexes with enzyme-labelled antibodies. They termed the technique ELIEDA (enzyme-linked immunoelectrodiffusion-assay) and found it useful to follow the immunologic evolution of hydatidosis and to identify IgM in ruptured hepatic cysts and IgA in pulmonary cysts.

Since the arc 5 antigen is diagnostic for infection with *Echinococcus*, the availability of this purified antigen makes the ELISA a very sensitive method for the serodiagnosis of hydatid disease.

### Nematodes

The first application of the ELISA for the diagnosis of infections with nematode animal parasites was reported by Ljungstrom et al (1974) and Ruitenbergh, et al (1974a, 1974b). They found that pigs with trichi-



nosis had detectable antibodies in their serum by 3 days of infection, further supporting the sensitivity of this assay. Further excellent studies on standardization and mechanization of the assay has resulted in a highly reproducible test that can examine 4,000 sera daily by only 2 individuals (Ruitenbergh, et al, 1975, 1976, 1977). Saunders, et al (1977) found that serum samples from all of 56 swine naturally infected with *T. spiralis* at a level considered dangerous to man were positive, whereas only one of 360 packinghouse sera negative for *T. spiralis* was positive by ELISA. Engvall and Ljungstrom (1975) have found the ELISA sensitive in detecting antibodies in infected humans.

Ruitenbergh et al (1977) found the ELISA to be more sensitive than IIF in detecting infections of *Toxocara canis* in cynomolgus monkeys.. Cypess et al (1977) found that the sera of patients with visceral larva migrans (VLM) caused by *T. canis* all had high antibody titers to the larva when tested by ELISA. The significant, specific antigen was obtained from embryonated eggs containing second-stage larvae. Glickman et al (1978) found the ELISA to be the method of choice over IHA, bentonite flocculation, and Ouchterlony immunodiffusion for the serodiagnosis of VLM. Schantz et al (1979) found that the prevalence and mean titers of *Toxocara* antibody detected by ELISA were greater in patients with ocular toxocariasis (OT) than for the control group, but not all clinically diagnosed OT cases had detectable antibody. Glickman et al (1979) demonstrated by ELISA *Toxocara*-specific antibodies in serum and the aqueous humor of a patient with presumed ocular and visceral toxocariasis.

Regarding use of the ELISA for the serodiagnosis of infections with nematodes, the mechanization of the technique has made it possible to detect low levels of infection in

swine in Holland and is being used as a routine method of surveillance and control in that country. The availability of an antigen from embryonated eggs *not* present in unembryonated eggs of *Ascaris* and *Toxocara* has made it possible to detect antibody in patients with ocular toxocariasis, whereas previous to the use of ELISA such cases were undiagnosable by serology.

### Concluding Comments

The quantitative nature of the ELISA and its high sensitivity gives the test tremendous advantages for the serodiagnosis of parasitic infections. However, the test requires a great deal of care in its standardization. For each test system, some of the parameters which need to be evaluated include:

1. purity and stability of antigen.
2. purity and quality of antibody conjugate.
3. type of conjugate.
4. type and quality of plate.
5. substrate used.
6. quality of reagents and buffers.
7. incubation and washing times.

### Acknowledgements

These studies were supported by NIH Grant No. RR-8102-08 administered by the Division of Research Resources, and by a grant from the Edna McConnell Clark Foundation.

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# Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

## Immunizations Halt Many Killer Diseases

### Vaccines Fight Ills

Immunization is a priceless health asset. Vaccines to prevent smallpox, diphtheria, tetanus and typhoid fever have been available for many years. Whooping cough, polio and "flu" vaccines were later added to the list. And most recently we added vaccines to protect against measles, German measles and mumps.

Immunization produces such a light form of a disease that the body reacts against it without becoming sick. This is called active immunity. Passive immunity is acquired from injections of protective substances produced in the body of an animal or another person. Infants receive passive immunity from their mothers against most common infectious diseases their mothers have had, such as measles, and this immunity protects them during the first few months of life.



A pamphlet from the American Medical Association points out that before 1900 diphtheria was among the most dreaded diseases of infants and children. Early in the century diphtheria toxoid was developed to protect children against this mass killer. Diphtheria toxoid is customarily given to small children in combination with tetanus toxoid and whooping cough vaccine for the basis immunization of children against all three diseases.

Whooping cough killed many children before a potent vaccine was perfected in the early 1930's. Deaths continue to occur where vaccination is neglected.

Tetanus immunization is of growing importance, the AMA pamphlet indicates. Tetanus germs, which lie dormant in the soil, may contaminate wounds sustained in auto accidents, sports, gardening, natural disasters, fires or explosions. Booster doses are needed every ten years or whenever a wound that could be infected occurs more than a year after immunization.

The Sabin oral polio vaccine is administered by mouth on a lump of sugar or in sweet liquid. A booster dose of the combined Sabin vaccine after 12 to 15 months and on entering school insures immunity to all three polio viruses.

August, 1978

Frank Chappell  
Science News Editor

A M A

# IT'S HIGHLY RECOMMENDED... AND FOR GOOD REASONS



Polymyxin B

Neomycin

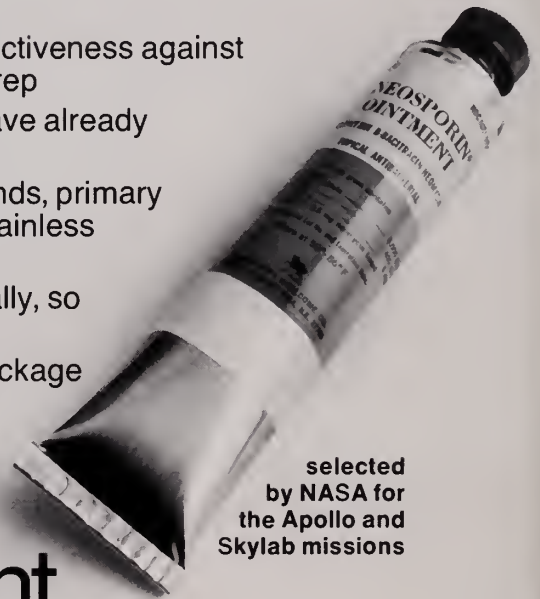
Bacitracin

Gram-negative  
Pseudomonas  
Hemophilus  
Klebsiella  
Aerobacter  
Escherichia  
Proteus  
Gram-positive  
Corynebacterium  
Staphylococcus  
Streptococcus  
Pneumococcus

1. provides broad-spectrum, overlapping antibacterial effectiveness against common susceptible pathogens, including staph and strep
2. helps prevent topical infections, and treats those that have already started
3. it's good medicine for abrasions, lacerations, open wounds, primary pyodermas, secondarily infected dermatoses; and it's painless and cosmetically pleasing
4. contains three antibiotics that are rarely used systemically, so the risk of sensitization is minimal
5. you can recommend it in any of the three convenient package sizes: 1 oz tube, 1/2 oz tube, or the versatile, single-use foil packet

## NEOSPORIN<sup>®</sup> Ointment

(polymyxin B-bacitracin-neomycin)



selected  
by NASA for  
the Apollo and  
Skylab missions

Each gram contains: Aerosporin<sup>®</sup> (Polymyxin B Sulfate) 5,000 units, bacitracin zinc 400 units, neomycin sulfate 5 mg (equivalent to 3.5 mg neomycin base); special white petrolatum qs; in tubes of 1 oz and 1/2 oz and 1/32 oz (approx.) foil packets.

**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, neomycin should not be used. One application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

**PRECAUTIONS:** As with other antibacterial preparations,

prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

**ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709



# KIDNEY STONES: A MEDICAL APPROACH

Laura E. Lespier-Dexter, MD

**Summary:** Nephrolithiasis is a common medical disorder. A pathogenetic mechanism can be identified in some patients. Thiazides, thiazides with allopurinol with moderate sodium restriction has proven to be a reasonable approach for prevention. The pathophysiologic mechanisms identified do not explain in full this condition because of its heterogeneity; more studies will be needed in order to answer the questions that are unresolved.

**Resumen:** Las piedras renales constituyen un problema médico común. El mecanismo patogenético se puede identificar en algunos pacientes. Las tiazidas, allopurinol o ambos han probado ser de utilidad en la prevención. Los mecanismos patofisiológicos que se han identificado no explican esta condición debido a su heterogeneidad, hacen falta estudios para resolver los múltiples interrogantes.

## Introduction

Recurrent nephrolithiasis is a common disorder in the Puertorican population. It constitutes a frequent cause of morbidity, disability, human suffering, loss of productivity, concurrent loss of income, use of medical facilities and expense.

Traditionally, this condition was considered solely within the realm of the urologist as a purely surgical condition in which other forms of medical therapy were ineffective. Recent data has shed light into the pathophysiologic mechanism of urolithiasis and has made medical therapeutic intervention feasible in some cases. The purpose of this review is to consider a medical approach to nephrolithiasis, pathogenesis, practical diagnostic work-up and preventive treatment.

## Pathophysiology

Three important theories have been proposed in order to explain the formation of stones: one emphasizes the existence of a matrix around which crystals precipitate; secondly, absence of a naturally occurring inhibitor has been proposed and thirdly, supersaturation leading to crystal formation (1, 2).

Three fourth of urinary calculi are composed of calcium oxalate (pure calcium oxalate, or calcium oxalate mixed with calcium phosphate). Five percent are made of calcium phosphate. Approximately 10-15 percent of stones are predominantly urate, associated with urine supersaturation with uric acid. Some of the calcium stones may contain urate and its presence facilitates calcium stone formation(3). A small percentage are cystine stones. The remaining fraction of patients will have stones in association with infection, (composed of magnesium - ammonium - phos-

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*From the Medical and Research Services, San Juan Veterans Administration Center and Department of Medicine, University of Puerto Rico School of Medicine.*

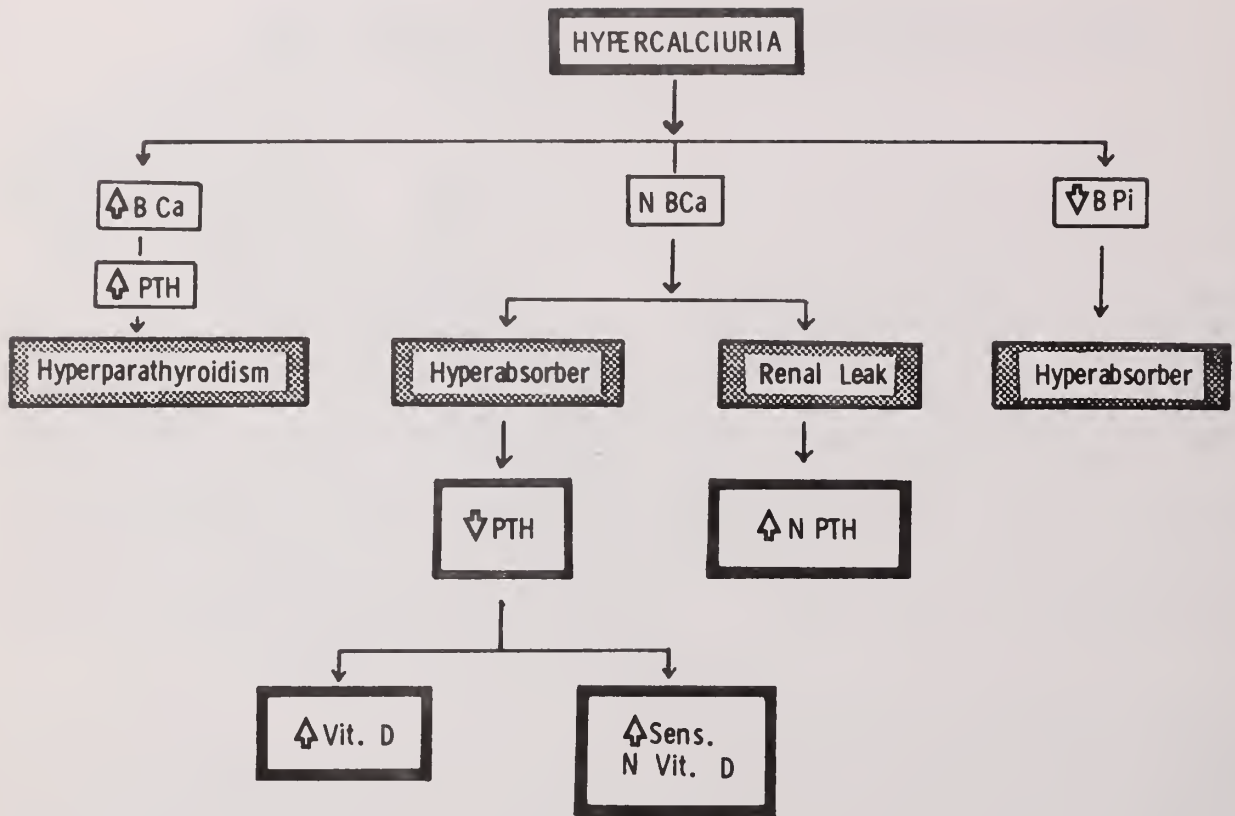


Figure 1 - Abbreviated representation of characteristics and mechanisms of idiopathic hypercalciuria in nephrolithiasis.

phate) and staghorn calculi (2).

In this discussion we will consider the most common types of stones. Calcium stone formers may fall into one of two main groups: hypercalciurics or normocalciurics. (2). Normocalciurics are those in whom an absent inhibitor or facilitatory environment for crystallization exists. Hypercalciurics may be associated with an identifiable metabolic disorder such as primary hyperparathyroidism with hypercalcemia, Cushing's syndrome, hypoparathyroidism, renal tubular acidosis, sarcoidosis, or with excessive calcium in the urine, as it occurs with excessive calcium, vitamin D or alkali intake. However, the vast majority

of calcium stone formers will be considered idiopathic hypercalciurics in whom no immediate cause is identified. Among this group we can identify 3 subgroups: (Fig. 1) absorptive, resorptive, reabsorptive (4,5). In the absorptive type there is increased gastrointestinal calcium absorption due to an increase in vitamin D activity or sensitivity (6) with a resultant depression of parathyroid function. Resorptive hypercalciuria is that associated with increased parathyroid function and increase bone calcium turnover, without hypercalcemia. The reabsorptive hypercalciuria is characterized by a defect in renal reabsorption of calcium or "renal leak" associated with chronic ne-

TABLE I

Basic Workup

Blood

*Calcium*

*Phosphorus*

*Creatinine*

*Uric Acid*

*Electrolytes*

Urine

*Urinalysis*

*ph*

*Culture*

24 Hrs. Urinary Collection for 3 days

*Calcium*

*Creatinine*

*Uric Acid*

Radiologic Studies

*KUB*

*IVP*

gative calcium balance that may eventually lead to a hyperparathyroid state.

Diagnostic Evaluation

Patients with nephrolithiasis should have a complete medical history and physical examination. Basic laboratory work-up is shown in Table I. An elevated blood calcium level should be considered evidence of hyperparathyroidism and lead to a complete parathyroid evaluation and referral for surgery. Nor-

mocalcemia is the most common finding in urolithiasis. Hypophosphatemia suggests hyperparathyroidism or "renal phosphate leak" associated with hyperabsorption of calcium (7). Creatinine and creatinine clearance are indexes of renal function. An elevated blood uric acid may be associated with uric acid stones and gout; uricosuria is associated with uric acid stones and facilitates calcium stone precipitation (3). Serum electrolytes may indicate renal tubular defects such as renal tubular acidosis in the presence of low bicarbonate and high chloride levels. The urina-



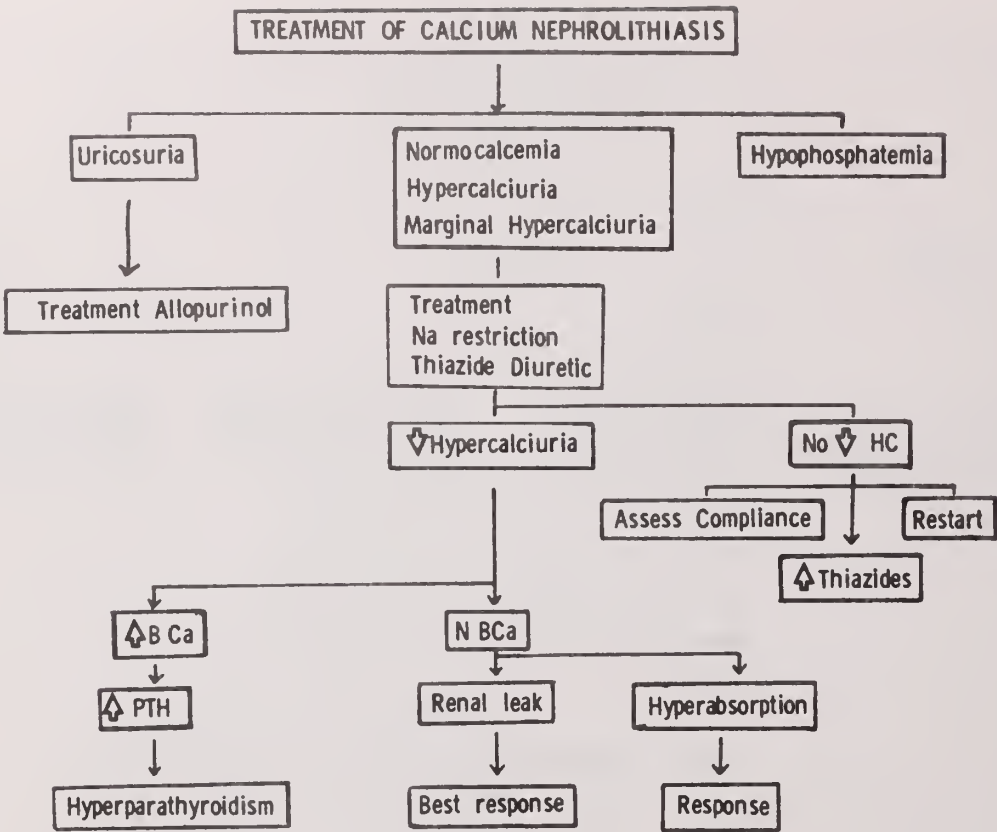


Figure 2 - Proposed treatment schedule and response.

lysis may show crystals, bacteria or cells. It may suggest abnormalities in tubular function or infection with urea splitting organisms if persistently alkaline.

Hypercalciuria is the most important risk factor associated with calcium stones (8, 9). Traditionally, it has been defined as a calcium excretion of more than 250 mg/24 hrs. for women and 300 mg/24 hrs. for men or more than 4 mg/kg/24 hrs. Nevertheless, hypercalciuria can only be defined as abnormal in relation to a calcium intake (10) and in relation to the population under study. For male Puerto Ricans, studied on an ambulatory basis, we have defined hypercalciuria as a calcium excretion of more than 220 mg/24 hrs. This value was established from the analysis

of 100 ambulatory unselected males, without problems in calcium metabolism studied while on a non regulated "Puertorican diet" with a calcium content of 800 mg, assessed by dietary history. (Unpublished observation)

Measurement of iPTH or its renal effector adenylyl cyclase (cAMP) should be considered special studies that permit, in conjunction with an acute calcium tolerance test further discrimination as to the pathophysiology of hypercalciuria (4, 5, 11). Nevertheless, these determinations are not generally required for management and should be reserved for selected cases. Measurement of urinary oxalate should be obtained only in patients with history of bowel disease. All patients should have a search for urinary infection. The pre-

sence of calcium stones can be determined by a plain abdominal film. Obstruction can be determined by ultrasonography. Obstruction, radioluscent stone or congenital anomalies should be evaluated by intravenous pyelography.

Patients with a first episode of stones may never pass another but since this is unpredictable, a first episode warrants complete evaluation. The above evaluation can be performed on an ambulatory basis in view of the high cost of hospital stay.

### Treatment

Patients with recurrent nephrolithiasis should be offered the alternative of medical treatment for prevention; conservative measures such as fluids and empiric dietary calcium restriction have not proven effective. Since abnormal calcium excretion or hypercalciuria is considered a risk factor maneuvers that chronically blunt calcium excretion should be beneficial (12). The methods most commonly used for this purpose are phosphate salts (13) or thiazide diuretics (12, 14). The relative beneficial effect of these is still controversial and subject of individual preference. Phosphate may be beneficial for the hyperabsorbers but a prospective controlled study failed to show a significant effect (13), therefore, it should only be considered for the small group of hypophosphatemic subjects for those with severe hyperabsorption or who have contraindications for other forms of therapy.

Multiple studies (12, 13) have shown the beneficial effect of thiazides and thiazides-allopurinol in the prevention of recurrent stones (Fig.2). Thiazides in the presence of a moderate sodium restriction of 87mEq lowers urinary calcium by increasing proximal renal tubular reabsorption of calcium and possibly by inhibiting hyperabsorption in some. Thia-

zides decrease urinary oxalate and increase inorganic phosphate, increase urine volume and prevent oversaturation. It has proven effective in both renal and absorptive hypercalciuria (14, 16), although, response may not be as dramatic in the latter. Moreover, it has proven effective even in patients with "marginal" hypercalciuria of 150 mg/24 hrs. The aim of therapy is to lower the urinary calcium excretion to values 25 percent or 50 percent of baseline or below hypercalciuric levels; this is achieved by careful titration of the thiazide. Indications for starting treatment should include: recurrence of calcium stones within a short period, and/or positive radiologic evidence of stone activity in the presence of hypercalciuria above 150 mg/24 hrs. Contraindications for thiazide therapy are a low arterial blood pressure, transient ischemic attacks, severe arteriosclerotic heart disease or conduction impairment, severe renal impairment, liver disease and hypersensitivity. Hypokalemia can be easily controlled with supplementation. The aim of therapy should be discussed and accepted by the patient.

Allopurinol is indicated for any recurrent Puertorican stone former with uricosuria of more than 600 mg/24 hrs., proven uric acid stones or mixed calcium-uric acid stones. (Unpub.)

Patients who develop hypercalcemia on thiazides should be searched for hyperparathyroidism.

Dietary calcium restriction may be added to those resistant to thiazides. General measures such as high fluid intake, treatment of infection and surgical intervention when indicated, are of importance.

Subjects selected for treatment should have serum electrolytes reevaluated shortly after onset of treatment and followed every 3 to 6 months thereafter.

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CONTESTACIONES (MEDI-QUIZ)

- 1. A, B
- 2. A, B
- 3. A, B
- 4. A, B, H
- 5. A
- 6. C
- 7. C
- 8. D
- 9. G
- 10. E
- 11. E, F
- 12. H



# INSIDIOUS METHYL ALCOHOL POISONING

Sidney Kaye, MSc, PhD

**Summary:** What was first thought to be a serious outbreak of food poisoning in Ponce, resulted in at least seven deaths. These cases were referred to the Institute of Forensic Medicine (University of Puerto Rico, Medical Sciences Campus) for general screening for poisons. It was then discovered that this sudden outbreak was due to methanol poisoning.

To be better prepared in the event of another similar incident (here or elsewhere) aids to rapid diagnosis, rapid simple tests for chemical identification, and suggestions for specific treatment have been outlined.

## Introduction

Methyl alcohol is a very *common* industrial chemical and yet intoxication and its dangers are not always easily diagnosed and recognized. The need for *early* diagnosis is very important because a *specific* antidote is available to us to minimize danger of blindness, and other damage and even to prevent death.

Since methyl alcohol is so commonly used by many; and since the occasional foolish "imbiding" can produce small or even massive outbreaks as have occurred from time to time in Atlanta, Georgia (1), Colombia, S. A. (2), Ponce, P. R. (3), and elsewhere, the

following is offered as a brief resume of some of the sources of exposure, properties, toxicity, signs and symptoms, detection, diagnosis, and specific treatment and general management in man.

"On the spot", rapid and simple and reliable presumptive tests\* are also included with the hope that one of these tests will be available to aid rapid diagnosis in your nearby general hospital. This test could now give you quick support and confidence in your diagnosis which would not have to await laboratory results from a great distance before instituting "specific treatment".

## Methyl Alcohol $\text{CH}_3\text{OH}$

**Synonyms:** Carbinol, methanol, wood alcohol, wood spirits, wood naphtha, Columbian spirits, Colonial spirits.

**Uses:** To make formaldehyde, auto anti-freeze (temporary-type), to denature alcohol, degreaser, organic solvent, organic dyes, fuel, paints, varnishes, enamels, embalming fluid, rubber accelerants, inks, canned heat, linoleum, lithographs, etc.

**Properties:** Colorless, clear, liquid, pleasant odor, bp  $64^{\circ}\text{C}$ , flammable, miscible with water.

*From the Institute of Forensic Medicine, School of Medicine, University of Puerto Rico.*

*Reagents will be supplied free of costs by the Institute of Forensic Medicine.*

*MLD*: About 75 ml/70 kg person; may vary widely due to tolerance (5).

*Remarks*: Can be absorbed thru all portals; Shellacking (painting) in an enclosed area (submarine), also by skin absorption; but poisoning is more serious when ingested. Although it is *acutely* less toxic as an *initial* CNS depressant than is ethanol, it is in fact far more toxic to man because of its metabolites, formaldehyde and formic acid. Methanol is first metabolized by alcohol dehydrogenase (ADH) to formaldehyde. The formaldehyde is then metabolized by oxidases to formic acid. This formic acid persists because it cannot be further detoxified by the Krebs cycle. Elimination may take about 5 to 10 times longer than ethanol. Although death can be within 5 hours (rapid), if massive quantities were taken (profound CNS depression), more often death is due to the delayed *severe metabolic acidosis* that depletes the alkali reserve, and disturbs the electrolyte balance.

*Symptoms (Acute)*: *Mild exposure* from inhalation or ingestion of small amounts: Headache, nausea, vomiting, irritation to all membranes, roaring and ringing in the ears, tiredness, insomnia, vertigo, diplopia.

*Severe exposure*: All above but more profound; plus abdominal pains, colic, GI irritation, diarrhea, constipation, lethargy, profound CNS depression, sleepiness, stupor, dizziness, dilated pupils, diplopia, cerebral edema, pulmonary edema, delirium, coma, profound metabolic acidosis due to metabolite formic acid. Edema of the optic nerve and entire retina (action of formaldehyde) with temporary blindness which can develop into permanent blindness if not *promptly* corrected. Imbalance of electrolytes with its serious complications; CNS degenerative changes, liver and kidney involvement.

*Prolonged chronic* environmental exposure may produce pulmonary edema, diplopia, possible involvement of the CNS, liver and kidney, etc.

*Identification* (Separated by steam distillation or by Trichloroacetic acid protein precipitation).

I. In blood, urine or steam distillate: To 2 ml of blood, to which an anticoagulant has been added (except EDTA or heparin), add 4 ml of trichloroacetic acid (20 percent); shake to precipitate proteins. Filter and collect clear filtrate.

To 0.1 ml of filtrate in a test tube, add 2 drops of potassium permanganate reagent (3 gm  $\text{KMnO}_4$  + 15 ml  $\text{H}_3\text{PO}_4$  + 85 ml of ether). Wait exactly 2 minutes and decolorize excess potassium permanganate with a pinch (size of a pin head) of sodium bisulfite. Add a pinch (size of a match head) of chromotropic acid (EK No.P 1613), and mix into a solution by swirling. Then carefully add 3 ml of sulfuric acid and mix. A purple color is *positive* for methyl alcohol. If you require a quantitation: Allow to stand for 20 minutes to *fully* develop color and then read in a spectrophotometer at 570 nm. With sulfuric acid as the reference blank and a 1 cm light path, the following calibration curve may be approximated. Each should prepare his own calibration curves with sulfuric acid as reference blank and a reagent control blank.

Methyl alcohol (gm %)	Transmission
0.025	55 % T
0.050	36 %
0.075	25 %
0.100	17 %

*Notes on the method*:

(a). This test is *very sensitive* when water

is excluded; and will even pick up trace amounts of methyl alcohol in the blood (0.001gm per cent). Low levels may not be clinically significant; however, trace amounts should be re-analyzed using a larger specimen (1 ml of filtrate).

(b). Always parallel a reagent blank at the time of testing the unknown. Occasionally the blank may give a strong positive test, especially when the test is performed in a laboratory where formalin is used. An open bottle of sulfuric acid has a great affinity for traces of formalin in the atmosphere.

(c). Formalin, heparin, methenamine and EDTA also give a positive test. Heparin or EDTA therefore cannot be used as the anticoagulant for blood. Autopsy tissue also can become contaminated in the autopsy room. Maximum precaution must be taken.

(d). To prove that the reaction is due to formalin, omit the (oxidation) potassium permanganate step and the test will still be positive; whereas methanol requires this (2-minutes)  $\text{KMnO}_4$  oxidation to be positive (for formaldehyde).

(e). Large amounts of ethyl alcohol may sometimes give a light brown color, but this is distinctly different from the deep purple of methyl alcohol.

(f). The presence of any amount of methyl alcohol above 0.05 per cent must be further studied and correlated with signs, symptoms, and history. It is imperative to perform the determination for carbon dioxide combining power of blood. It is the degree of *acidosis* which is of primary consideration in treatment.

(g). Since methyl alcohol is metabolized and eliminated slowly, it may be found in the

blood as long as 6 days later. Traces may also be found when large amounts of wine have been consumed.

II. Into 10 ml of distillate, plunge a red-hot copper spiral \* eight times. (Gettler) (6).

a. To 5 ml of this oxidized solution add 10 drops of 0.5 percent (fresh) phenylhydrazine hydrochloride, then 2 drops of 0.5 percent sodium nitroprusside, and then 10 drops of 20 percent sodium hydroxide. Blue  $\rightarrow$  green  $\rightarrow$  yellow  $\rightarrow$  red-violet color indicates presence of formaldehyde (oxidized methyl alcohol).

b. To 5 ml of this oxidized solution; add 2 ml of sulfuric acid and 5 ml of reduced fuch-sine solution. A violet color is developed in a couple of minutes. This color can be quantitated.

Fuch-sine solution: 0.2 gm of basic fuch-sine is added to 150 ml of boiling water. Dissolve and then cool with running water. Two grams of sodium bisulfite (mets) in 20 ml of water is added and mixed. Then add 2 ml of hydrochloric acid and 60 ml of water. Mix and store in a glass-stoppered dark bottle. This solution should be stored in a refrigerator and will be stable for many months.

c. Microdiffusion as for ethanol (6).

d. Gas chromatography (if available) (6).

*Treatment:* Immediate gastric lavage with sodium bicarbonate, or emetics for quick evacuation, if patient is not comatose. Cathartics

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Twist a thick copper wire around a pencil up to about 12 spaces. Use cork or rubber stopper to insulate for handling.



such as sodium sulfate (25 gm). Keep patient warm and quiet. Protect eyes from strong light. Maintain electrolyte and water balance. Acidosis is to be prevented or corrected if treatment is to be successful. The carbon dioxide combining power and the electrolytes should be determined initially and then repeated at intervals to evaluate response to treatment (and seriousness of poisoning).

Sodium bicarbonate intravenously, slowly until acidosis is corrected. Treatment with bicarbonate should be continued for several days as needed, with careful evaluation.

Hemodialysis if available would materially hasten elimination of both methyl alcohol and formic acid (in severe cases).

Ethyl alcohol 50 percent orally (5-20 ml) every 2 to 4 hours may help slow down conversion of methyl alcohol to the more toxic formaldehyde and formic acid by competing for the same metabolic enzymes (ADH).

Supportive measures to maintain vital signs; glucose and fluids; Vitamin B<sub>1</sub> for visual disturbances; guard against secondary infections if patient is comatose. Symptomatic and supportive measures.

### Appendix (7)

NIOSH recommended standard for occupational exposure to methyl alcohol: 200 parts per million (ppm); 262 mg per cubic meter

of air as a time-weighted average for up to a 10 hour work day, 40 hour work week. In addition NIOSH recommends a ceiling of 800 ppm; 1, 048 mg per c.m. of air as determined by a sampling time of 15 minutes.

Approximately one billion (1,000,000,000) gallons of methyl alcohol were used by industry in 1973. NIOSH estimates that approximately 175,000 workers in the USA are potentially exposed to methyl alcohol.

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Pale green 300 mg. tablets  
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**When painful spasm  
is the presenting  
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...in the functional bowel/irritable bowel syndrome\*

# Bentyl<sup>®</sup>

## (dicyclomine hydrochloride USP)

10 mg. capsules, 20 mg. tablets,  
10 mg./5 ml. syrup, 10 mg./ml. injection

helps control abnormal motor activity  
with minimal anticholinergic side effects†

### Demonstrated smooth muscle relaxant activity.

In this double-blind study, twenty patients having G.I. series and exhibiting spasm were randomly selected to receive either 2 cc. of Bentyl or sodium chloride intramuscularly. Ten minutes after the injection another radiograph was taken . . .

. . . Bentyl produced definite relaxation in 8 of 10 patients. The sodium chloride produced relaxation in only 3 of 10. No side effects occurred in either group of patients.



Pylorospasm has almost totally blocked passage of barium meal.



Barium meal beginning to pass 10 minutes after intramuscular injection of 20 mg. Bentyl.

*"The correlation of spasm relief and drug given was excellent."*

\*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

#### Reference:

King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

# Merrell

# Bentyl<sup>®</sup>

(dicyclomine hydrochloride USP)

Capsules, Tablets, Syrup, Injection

AVAILABLE ONLY ON PRESCRIPTION

Brief Summary

#### INDICATIONS

Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the following indications as "probably" effective.

For the treatment of functional bowel/irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis.

THESE FUNCTIONAL DISORDERS ARE OFTEN RELIEVED BY VARYING COMBINATIONS OF SEDATIVE, REASSURANCE, PHYSICIAN INTEREST, AMELIORATION OF ENVIRONMENTAL FACTORS.

For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

**CONTRAINDICATIONS:** Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage; severe ulcerative colitis; toxic megacolon complicating ulcerative colitis; myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with: Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. **ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia; urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis, urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSEAGE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

**Usual Dosage.** Bentyl 10 mg. capsule and syrup: *Adults:* 1 or 2 capsules or teaspoonfuls syrup three or four times daily. *Children:* 1 capsule or teaspoonful syrup three or four times daily. *Infants:* ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg.: *Adults:* 1 tablet three or four times daily. Bentyl Injection: *Adults:* 2 ml. (20 mg.) every four to six hours intramuscularly only. **NOT FOR INTRAVENOUS USE. MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine<sup>®</sup> (bethanechol chloride USP) should be used.

Product Information as of October, 1978.

Injectable dosage forms manufactured by CONNAUGHT LABORATORIES, INC., Swiftwater, Pennsylvania 18370 or TAYLOR PHARMACAL COMPANY, Ocaturo, Illinois 62525 for MERRELL-NATIONAL LABORATORIES, Division of Richardson-Merrell Inc., Cincinnati, Ohio 45215, U.S.A.

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## USO EXPERIMENTAL Y CLINICO DE INJERTOS VASCULARES DE POLITETRAFLOROETILENO

*Hace ya más de 25 años que se introdujo en el armamentario quirúrgico el uso de injertos vasculares contruídos de tejido artificial. Anteriormente, la única manera de reparar arterias desgarradas, obstruídas, o enfermas era mediante el uso de tubos rígidos o de alo-injertos arteriales o venosos. Recordamos que la inmensa mayoría de estos intentos iniciales fallaron ya que la activación de los sistemas inmunológicos y de coagulación resultaba en daño irreparable del injerto, y en la década de 1950 se abrió un nuevo campo que permitió restaurar irrigación sanguínea a órganos y extremidades.*

*Los injertos tejidos con que contamos hoy día sufren todos de limitaciones que los hacen imperfectos. En primer lugar, existe el problema de coagulabilidad y de turbulencia. Además, los injertos existentes son duros y relativamente rígidos y hacen su inserción técnicamente incómoda y muchas veces difícil. En adición a ésto, la mayoría de ellos requieren arterias de alto flujo, y su uso para substituir vasos pequeños es limitado.*

*En los últimos años se ha introducido un material nuevo en el armamentario quirúrgico. Esta substancia, politetrafloroetileno (Gore-Tex; PTFE), presenta propiedades que mejoran considerablemente los injertos previamente en uso. El PTFE no es nada más que una forma especial del Teflón (R), que se logra alterando algunas variables físicas durante su producción. Es muy suave, flexible, blando, relativamente poroso, de poca trombogenicidad, de fuerza uniforme en todo el tubo; causa muy poca toxicidad, y produce en los tejidos una inflamación mínima. Del 1972 al 1975 fue utilizado primordialmente como injerto para substituir venas y arterias intermedias. Del 1975 hasta esta fecha se han implantado más de 60,000 de estas unidades en los Estados Unidos y Puerto Rico, de los cuales hay datos concretos en 5,000 casos.*

*En el 1975 introdujimos este injerto para su uso en Puerto Rico (1). Inicialmente practicamos una serie de experimentos en perros, insertando injertos de 6-8 milímetros para substituir pequeños segmentos de aorta o para hacer anastomosis aortoiliacas. Los parámetros médicos fueron: la facilidad de uso técnico, la patencia, y la interacción con los tejidos. Encontramos que la manipulación y el uso técnico del injerto era muy sencillo, y que era notable la facilidad con la cual las anastomosis se podían hacer. También fue notable la facilidad del material de adaptarse a las formas de los tejidos. Encontramos particularmente atractivo el hecho de que el PTFE no necesita coagulación anterior. Seis de siete (6/7) injertos estaban patentes al terminar el período de observación, en comparación a cuatro de siete (4/7) injertos de Dacrón que usamos como control. De interés fue el encontrar que la reacción inflamatoria (vista macro y microscópicamente) en y alrededor del injerto era mínima en comparación con aquella producida por los injertos existentes.*

*Satisfechos con estos experimentos y basándonos en informes preliminares en la literatura, comenzamos a usar el injerto de PTFE como acceso vascular para pacientes con problemas arteriales*



y que necesitan hemodiálisis. Nuestra experiencia incluye 24 injertos en 21 pacientes. La primera opción para acceso vascular en un paciente con insuficiencia renal terminal lo es la fístula arterio-venosa. Si la diálisis se necesita de emergencia, implantamos entonces una cánula externa de Silastic. Con frecuencia nos encontramos con pacientes que tienen problemas arteriales o venosos, o en quien se han agotado las posibles vías de acceso vascular, bien sea por trombosis, cirugía previa o fibrosis. Anteriormente utilizábamos autoinjertos de vena safena o injertos pretratados de arteria carotídea bovina.

Al analizar este estudio clínico, encontramos la misma facilidad de inserción, patencia e interacción con los tejidos que observamos en experimentos anteriores. La mayoría de los injertos están patentes aunque hemos tenido que reoperar tres injertos debido a sangría o a obstrucción venosa, y hemos removido tres injertos por infección (dos) y obstrucción (uno).

Nuestra experiencia hasta el presente nos hace concluir que este nuevo material es, por lo menos igual, y probablemente mejor que los materiales existentes en cuanto a facilidad de uso, patencia e interacción con los tejidos. En pacientes difíciles con vasos sanguíneos dañados, es nuestra primera selección como acceso vascular para hemodiálisis. Hace varios años que no utilizamos el injerto de vena safena o de arteria bovina para este propósito.

Eduardo A. Santiago Delpín, MD  
Director, Programa de Trasplantes

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**ABSTRACTOS: REGIONAL MEETING  
AMERICAN COLLEGE OF PHYSICIANS  
OCTOBER 19-20/79**

**EXPERIENCES WITH MALIGNANT EXTERNAL OTITIS: A NEW COMPLICATION OF DIABETES MELLITUS**

*Velia Toledo, MD, Vicens Enrique, MD, Rodríguez Ismael, MD-  
The Medicine and ENT Departments, Damas Hospital, Ponce,  
Puerto Rico.*

Malignant External Otitis is a severe infection which occurs in the elderly diabetic patient. It results in unremitting pain, purulent discharge and tends to invade cartilage, bone nerves and adjacent soft tissues. The causative agent is almost uniformly *Pseudomonas aeruginosa*. It may be responsible for cranial nerves palsies, meningitis and death. Our series consist of 14 patients with Malignant External Otitis. In 12 of them Diabetes Mellitus preceded the onset of the complication, in 2 patients were on dietary therapy alone, 3 were using oral agents; 7 were on Insulin therapy and 2 were in combination therapy. *Pseudomonas aeruginosa* was cultured in 13 patients and *Citrobacter Diversus* was cultured in one. Systemic broad spectrum antibiotics were administered to all of the patients. Twelve patients required some type of surgical treatment (debridment, drainage, radical surgery) while one refused surgery and one had a biopsy only for diagnostic purposes. Among the complications found, there were 5 patients who showed neurological involvement such as cranial nerve palsies (VII, VIII, IX, X, XI) either alone or in combination; meningitis and brain abscess in one, mastoiditis in 4 patients. There were 3 deaths as a result of the disease (21.5 percent). Eight patients are alive and free of disease, and 3 patients the status is unknown.

**PENICILLIN SUSCEPTIBILITY PATTERNS OF GINGIVAL ORGANISMS OF RHEUMA-**

**TIC FEVER (RF) PATIENTS (PTS) ON PROPHYLAXIS**

*B.. Christenson, MSIV, D. Vera, B.S.M.T., H. Delgado, MD, A. Martínez-Picó, MD and C. H. Ramírez-Ronda, F.A.C.P. - Div. Inf. Dis. and Cardiology Sect., Depts. of Medicine and Pediatrics UPR School of Medicine, San Juan, Puerto Rico.*

Prophylaxis with penicillin (P) for RF is an accepted procedure; it can be carried out with oral P (OP), benzathine P (BP) or erythromycin. It has been shown that patients (PTS) on OP prophylaxis have a higher number of P resistant (PR) viridans streptococci (VS) in their gingival flora. The finding of PR VS in the gingiva is an indication for modification of the bacterial endocarditis (BE) prophylaxis on such PTS. A study was designed to determine the number of PR VS in RF PTS on prophylaxis and to compare it to a control group. A total of 10 PTS on BP prophylaxis, 2 PTS on OP prophylaxis and 10 control PTS were studied. Gingival cultures were plated in a P medium and in nutrient agar (NA). All colonies grown in the P medium and 5 colonies of VS were selected at random from NA, identified, and the susceptibility to P and other antibiotics determined. A total of 110 organisms were studied, 10 from PTS on OP, 50 from PTS on BP and 50 controls. The number of PTS on OP prophylaxis was small, almost all PTS received BP as their prophylaxis. None of the colonies of VS studied from the PTS on BP prophylaxis was PR, only 1 of 50 colonies studied from the control group was PR. The number of PTS on OP was too small to detect any PR VS. The data demonstrates that prophylaxis with BP is effective in preventing the emergence of PR among oral VS. This practice should continue in Puerto Rico. PR VS on PTS on OP prophylaxis has been documented in other groups, and these PTS should have a modified BE prophylaxis regime. RF PTS on BP prophylaxis can receive the standard BE prophylaxis whenever they are orally

instrumented.

## FUNCTIONAL CHEMODECTOMA OF THE RIGHT ATRIUM: THE CASE OF THE MISSING PHEOCHROMOCYTOMA

*Francisco Aguiló Jr., MD, Eduardo de León, MD and Rosa Haiffe de Noriega, MD*

A 26-year-old negro female with marfanoid habitus became febrile after her last pregnancy which had been attended by hypertension and terminated in stillbirth. A non-descript neurological picture characterized by disorientation was ascribed to "cerebritis" due to sepsis after a D & C. CSF findings of pleocytosis (300 PMN), low glucose (25 mg/dL) and high protein (360 mg per dL) lead to presumptive Dx of tuberculous meningitis.

Two months post partum hypertension (220/150), tachycardia and marked postural hypotension were noted. A Regitine test was markedly positive (drop in BP to 90/60 in 30 secs). Urinary VMA was 12.5  $\mu$ g/mg creatinine normal < 6). Oral GTT was diabetic.

After treatment for recurrent meningitis, and a pulmonary embolus, exploratory laparotomy failed to reveal an adrenal tumor. For 2 years she was maintained on alpha-methyl dopa, 250 mg tid and chlorothiazide, daily. Final admission was prompted by nausea, vomiting, dizziness, weakness, a 7lb weight loss and marked nuchal rigidity, BP 160/100. After a final episode of pulmonary embolism she died.

Autopsy revealed a chemodectoma of the right atrium. Extraction of the tumor for total catecholamines showed 200  $\mu$ g per Gm of tissue (180  $\mu$ gME and 20  $\mu$ g Nepinephrine).

This is the second cardiac chemodectoma we are aware of (first one: Lahey Clin. Found Bull. 16: 224-229, 1967) and the first functional one.

## MORTALITY OF DIABETIC PATIENTS WITH ACUTE M. I.

*Gloria Rodríguez Quiñones (Associate), Ralph Conaway Lanuza, MD - Department of Medicine, San Juan City Hospital, San Juan, Puerto Rico.*

We reviewed 128 out of 242 patients who were admitted to Dan Juan City Hospital for acute myocardial infarction in the year 1976 to determine their incidence of short term cardiovascular complications and mortality. We found that 30 percent of these patients were diabetics and subdivided them in the following manner: diabetes de novo 27 percent, untreated 14 percent, Insulin 18 percent, diet 9 percent and oral hypoglycemic agents 32 percent. Of these, we found that those patients who were on oral hypoglycemic agents had twice as many complications and mortality as the other groups. We found that diabetics had a higher incidence (18 percent) of angina pectoris than non diabetics (12 percent) while the rest of the complications (heart failure, cardiac tamponade, embolism, arrhythmias, rupture, cardiogenic shock, re-infarction and pacemaker implantation) were not statistically significant. Non diabetics had a higher mortality (21 percent) as compared to diabetics (9 percent). This data contradicts other reports. We have found no evidence to suggest that diabetic patients are more prone to the effects of short term myocardial infarction complications nor mortality than their non diabetic counterparts.

## ACUTE MYOCARDIAL INFARCTION IN DIABETES MELLITUS

*Agustín M. de Andino, FACP and Gabriel Martínez Rovira, Member, Department of Medicine, San Juan City Hospital and Department of Medicine, Doctors' Hospital, San Juan.*

Last year we presented the results of a study on the causes of death in a series of 282 private diabetic patients followed for a period of 25 years. Vas-

## COMPARISON OF THE SHORT TERM CARDIOVASCULAR COMPLICATIONS AND



cular disease was responsible for 80 percent of the deaths with atherosclerotic heart disease accounting for 44 percent and cerebrovascular causes for 26 percent. Acute myocardial infarction was the most important cause of demise.

The present study attempts to elucidate the factors involved in the pathogenesis, mortality and survival in diabetic patients who develop an acute myocardial infarction. A total of 101 cases were studied during a 25 year period of time, 53 males and 48 females, 85 cases died and 16 survived. After the 1st infarction 65 patients died. 61 patients (60.3 percent) were insulin dependent diabetics and 58 of them died for a mortality of 95 percent.

There was no difference in the mean age of the treatment groups (Diet, Oral agents and Insulin).

The important risk factors in the whole series were a family history of heart disease, a previous cardiac history in the patient, and preceding electrocardiographic abnormalities. Of less importance were hypertension, lipid abnormalities, cigarette smoking and obesity. In the deceased group the incidence of the risk factors was the same as for the whole group.

There is no doubt from our study that the presence of diabetes mellitus in a patient with myocardial infarction makes the prognosis extremely poor and in direct relation with the severity of the metabolic disease.

## INITIATION OF REENTRANT TACHYCARDIA DURING PROGRAMMED ATRIAL OR VENTRICULAR STIMULATION

*Juan M. Aranda, MD, Migdalia González, MD, Esteban Linares, FACP, Guillermo Cintrón, FACP and Fernando Córdova, MD - Cardiology Section, Veterans Administration Hospital, UPR School of Medicine, SJ, PR*

The purpose of this study was to outline the mode of initiation and mechanism of paroxysmal supraventricular (PSVT) and ventricular tachycardia (VT) in patients (pts) referred to the Electrophysiologic Laboratory for evaluation of cardiac arrhythmias. His bundle, high right atrial and coronary sinus elec-

trograms were simultaneously recorded with several surface electrocardiographic leads. Of 11 pts with documented (9 pts) or suspected (2 pts) cardiac arrhythmias, 9 pts had sustained tachycardia induced during programmed atrial or ventricular stimulation. In all pts the tachycardia could be terminated with one or two consecutive mechanical induced atrial or ventricular contractions. Six pts (group I) had reentrant PSVT. The site of reentry was localized in the atrium in 1 pt (either the atrial myocardium or specialized atrial tract), the A-V node (intranodal), utilizing the A-V node for antegrade conduction and the Kent bundle for retrograde conduction. Three pts (group II) had sustained ventricular tachycardia. Although His-Purkinje reentry was intermittently observed in 1 pt, the electrophysiologic data suggested that reentry in the distal Purkinje system, Purkinje-myocardial junction or ventricular myocardium was the most likely mechanism of the rhythm disturbance. In our groups of pts, intranodal or extranodal reentry is the most frequent mechanism of PSVT. In those pts with recurrent VT, reentry in the distal Purkinje system, Purkinje-myocardial junction or ventricular myocardium is the most frequent mechanism observed.

## AMIKACIN SULFATE LEVELS IN HUMAN BILE

*R. H. Bermúdez, FACP, A. Lugo, MD, J. Morales, MD, J. H. Amadeo, MD, and C. H. Ramírez Ronda, FACP - VAH and UPR School of Medicine, San Juan, Puerto Rico.*

Antibiotic levels achieved in human bile are of therapeutic and pharmacokinetic significance. The objective of this study was to evaluate the penetration of amikacin into bile. Amikacin in bile and serum was measured by radioimmunoassay in ten patients (PTS) who underwent cholecystectomy and t-tube drainage. Every PT received 500 mg amikacin 12 hrs pre-operatively, during surgery (immediately after bile was obtained from common duct), and every 12

hrs. for four doses. Serum and bile were collected postoperatively at 1, 2, 6 and 12 hrs after every IV dose of 500 mg amikacin administered in 30 minutes. Amikacin bile levels of 8.3 ug/ml were measured 1 hr after the intraoperative dose with a bile/serum ratio (BSR) of 0.44. Amikacin dosages after postoperative doses administered every 12 hrs produced serum levels at 1 hr of 13.4-424.6 ug/ml with bile levels of 4.1-9.4 ug/ml and BSR of 0.2 to 0.69. Amikacin levels in serum decreased at 2 hrs (12-14 ug/ml), 6 hrs (4-6 ug/ml), and 12 hrs (1.3-2.2 ug/ml) while bile levels decreased at a lower rate 2 hrs (6-9 ug/ml), 6 hrs. (1.2-3.7 ug/ml) and 12 hrs (0.95-1.5 ug/ml), and the BSR increased, 2 hrs (0.55), 6 hrs (0.84), and 12 hrs (0.93). There was accumulation of amikacin in bile 6 hrs after IV dose. Amikacin penetrates the bile in concentrations that range from 4.1-9.4 ug/ml.

## UNUSUAL FINDINGS IN PATIENTS WITH CARDIAC ARRHYTHMIAS AND VENTRICULAR PRE-EXCITATION

Juan M. Aranda, MD, Mígdalia González, MD, Esteban Linares, FACP, Edgardo Hernández López, MD, Guillermo Cintrón, FACP - Cardiology Section, Veterans Administration Hospital, University of Puerto Rico, School of Medicine, San Juan, P. R.

The purpose of this study was to evaluate antegrade and retrograde conduction pathways in patients (pts) with documented complex cardiac arrhythmias and suspected ventricular pre-excitation. His bundle (HBE) and bipolar high right atrial (HRA), coronary sinus (CS) and right ventricular inflow tract (RVIT) electrograms were recorded simultaneously with various surface leads in 4 pts with supraventricular or ventricular rhythms and suspected Wolff-Parkinson-White syndrome (WPW) Type A.

The unusual responses to electrical stimulation in these pts included: a) supraventricular reentrant extranodal tachycardia with antegrade A-V nodal conduction and retrograde posterior accessory tract conduction with rate related LBBB mimicking anterior ventricular pre-excitation (Type B WPW) in the surface electrocardiogram (1 pt). b) atrial fibrillation with

fast antegrade posterior accessory tract conduction and retrograde block in the accessory tract, simulating ventricular tachycardia or ventricular flutter (2 pts). c) supraventricular reentrant intranodal tachycardia (dual A-V nodal pathway) and retrograde block in the posterior accessory pathway (1 pt). d) Mahaim tract conduction (short and constant H-V interval during atrial pacing) and accelerated idioventricular rhythm mimicking intermittent Type A WPW.

As a result of these unusual findings, drug therapy was modified in 3 of the 4 pts studied. Electrophysiologic and intracavitary recordings should be performed in pts with suspected ventricular pre-excitation and complex cardiac rhythm. Understanding these variations may provide important therapeutic implications.

## CYCLIC AMP IN THE DIAGNOSIS OF DISORDERS IN CALCIUM METABOLISM

Laura Lespier-Dexter, MD, Francisco L. Burgos, MD, Raul Marcial - Research and Med. Services, VA Hospital and School of Medicine, University of Puerto Rico, San Juan, Puerto Rico.

A number of technical and biological difficulties restrict the availability and reliability of parathyroid hormone (iPTH) determinations. Urinary and nephrogenous cyclic AMP (NcAMP) have been suggested to provide an optimal and easier method to assess parathyroid function and end organ response in situations associated with abnormal calcium metabolism. Studies were performed on five different groups of subjects under basal controlled conditions. Results were as follows:

Subjects	NcAMP(nmoles/100 ml GRF)
Group I - hyperparathyroids(HPT)	
(n=4)	6.36 ± 6.30
Group II - post surgical HPT	1.74 ± 2.11
Group III - hypoparathyroids	
(n=2)	0.12 ± 1.35
Group IV - pseudohypoparathyroids (n=3)	2.93 ± 1.49
Controls (n=19)	3.02 ± 1.35

Group I was significantly higher from any other group ( $p < 0.001$ ) and Group III was significantly lower from any other group ( $p < 0.001$ ). There was no significant difference among Group IV and controls. When hypocalcemic patients (group III and IV) were compared, a significant difference was evident ( $p < 0.01$ ). Surgically treated hyperparathyroid patients had lower NcAMP than Group I. Our data demonstrates that NcAMP gives an accurate, reproducible and sensitive index of parathyroid function in hypercalcemic states showing elevation if it is of parathyroid origin. In hypocalcemic states, permits discrimination between hypoparathyroidism and pseudohypoparathyroidism. NcAMP eliminates the need for the unreliable iPTH determination.

## **LIVER SCINTIGRAPHY IN ASYMPTOMATIC PATIENTS TAKING ORAL CONTRACEPTIVES**

*Frieda Silva, MD, Samuel Sostre, FACP, M. Kazmain Zaidi, MS and Aldo E. Lanaro, MD - University of Puerto Rico*

The increased incidence of hepatic adenomas and focal nodular hyperplasia in patients taking oral contraceptives (BCP), at times with life threatening complications, has been well documented. Liver spleen scans were performed on 56 patients taking oral contraceptives for 1-14 years and on 56 patients using other contraceptives methods, (control group), to evaluate the role of the liver scan in the early detection of focal hepatic lesions in asymptomatic patients using these medications. Early detection of these lesions may lead to rapid treatment and possibly the prevention of the known complications of these tumors.

Only one patient on oral contraceptives had focal hepatic defects and full evaluation revealed fatty metamorphosis and not a BCP associated lesion.

In addition, 24 abnormal scans were found on the BCP group and 18 on the non BCP users. These abnormalities included hepatomegaly, splenomegaly, and non-uniform tracer distribution. There was no statistical significance between the study and control groups concerning these abnormalities.

It is concluded that routine liver scanning in asymptomatic patients taking BCP has no clinical usefulness. When the cost of such a screening program is considered it becomes even less desirable procedure. Liver scan should be reserved for the patient on BCP presenting with symptoms suggesting hepatic disease.

## **ACUTE LUPUS CEREBRITIS WITH DEATH-A-SUBSET OF PATIENTS WITH SYSTEMIC LUPUS ERYTHEMATOSUS (SLE)**

*Braulio Quintero, MD, Rodolfo A. Concepción, MD, Russell A. Del Toro, MD - San Juan, Puerto Rico*

During the past 5 years we have studied 100 patients with Systemic Lupus Erythematosus (SLE). Twenty percent have had cerebral involvement with neurologic and or psychiatric manifestations. Three of these developed an unique clinical picture characterized by progressive somnolence, stupor, convulsions, coma and death in a few days, despite corticosteroid therapy in the usual high doses (60-80 mg of Prednisone daily). A short summary of each case will be presented.

The 3 patients fulfilled the ARA criteria for the diagnosis of SLE. All were teen-agers. Two were relatively mild cases of short duration (2-4 months) mainly joint and skin involvement. The third patient had arthritis and thrombocytopenic purpura of one year duration. None had significant renal disease nor hypertension. Pathologic findings, and specially those in the central nervous system were characteristically meager.

The fourth patient with a similar clinical picture but that doesn't fulfill the criteria for a definitive diagnosis of SLE, was also studied. This was the only survivor of the group but remains with severe neurologic residuals.

These conditions should be suspected in any young patient with SLE, specially in the mild case who starts complaining of somnolence. Immediate emergency studies should be done and the patient started in higher than usual dosages of steroid therapy.



## ROLE OF TEICHOIC ACIDS ON THE ADHERENCE (AD) OF STAPHYLOCOCCUS AUREUS (SA) TO DAMAGED CANINE AORTIC VALVES IN VITRO

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SA adheres well to normal and damaged heart valves *in vitro*. The AD of glucan-positive streptococci (SC) to heart valves is dependent on glucan production. SA does not produce glucans but adheres to heart valves. Teichoic acids (TA) have been shown to be important in AD of some SC to epithelial cells, SA have TA in their cell walls. A study was designed to see the effect of various concentrations of crude extract of TA on the AD of bacteremic strains of SA to damaged heart valves. Valve damage was produced in dogs by insertion of a polyethylene catheter to the left side of the heart. Measurement of AD was carried out *in vitro*. The AD was determined with damaged valve sections, before incubation with TA crude extract (TACE) and after incubation with various dilutions of TACE. TACE was obtained from the Lafferty strains of SA. Adherence ratios (AR) defined as the proportion of bacteria in each standardized bacterial suspension that adhered to each pair of valve sections were based on viable counts. The AD for SA G-4 under control conditions was  $2790 \pm 190$ , after 1 hr incubation with TACE the AR was  $390 \pm 46$ ; for SA CR-100 was  $2910 \pm 178$  control and  $496 \pm 94$  after incubation. The effect of various dilutions of TACE demonstrated that the inhibitory effect on AD of TACE for SA G-4 was present up to dilutions of 1:20 ( $602 \pm 70$ ); at 1:80 the effect was negligible ( $2180 \pm 76$ ). The adherence of 2 strains of SA was decreased significantly by TACE in dilutions of up to 1:20; this may be related to blockage of TA receptor sites. TA may play a role in adherence of SA to endothelial surfaces covered with fibrin and platelets.

## MYOCARDIAL INFARCTION WITH MYO-

## CARDIAL BRIDGING OF THE LEFT ANTERIOR DESCENDING CORONARY ARTERY WITHOUT CORONARY ATHEROSCLEROSIS

José Pérez Hernández, MD, Ralph Conaway, MD, José Fernández Martínez, MD, FACP, FACC, Marilyn Ríos, MD, and José Serrano Muñoz, MD, FACC, San Juan City Hospital, San Juan, Puerto Rico.

A 39-year old male patient underwent selective coronary arteriography for evaluation of chest pain four months after an acute anterolateral myocardial infarction. No fixed atherosclerotic lesions were found. Myocardial bridging of the proximal segment of the left anterior descending coronary artery resulted in a systolic reduction of the vessel size of 75 percent. During ventricular diastole the size and intimal contour were judged to be normal.

Ergonovine maleate in a dose 0.2 mg intravenously under continuous Coronary Care Unit monitoring failed to produce angina pectoris or ST segment deviations.

A case of anterolateral myocardial infarction confirmed by left ventriculography with no fixed stenotic coronary lesions and no demonstrable coronary vasospasm is presented. The role of myocardial bridging and possible local clot formation remains speculative.

## CORRELATION OF EARLY POST INFARCTION HEMODYNAMICS AND TREADMILL EXERCISE TESTING

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The purpose of this study was to correlate hemodynamic measurements obtained within 24 hours of

first acute transmural infarction (AMI) with treadmill testing (GXT) 3 months (mos) later. We studied retrospectively, 42 male veteran patients (pts) who underwent right heart catheterization within 24 hours of symptoms of AMI and performed GXT 3 mos later. Pts were divided in 2 groups (grp) according to pulmonary artery diastolic or pulmonary wedge pressures (PCW). Grp I: PCW < 12 mm Hg., 16 pts; Grp II: PCW > 12 mm Hg., 26 pts. Both grps were comparable regarding age and history of prior congestive heart failure. In Grp I pts, 15/16 had inferior AMI, mean peak creatine phosphokinase (CPK) was 839 IU and 68 percent (11/16) had hypertension by history. In Grp II pts, 23/26 had anterior AMI, mean peak CPK was 1336 IU and 35 percent (9/26) had hypertension by history.

Results of 3 mos GXT were as follows:

	GXT(+)	GXT(-)	±*
Grp I (16)	4(25°/o)	5(31°/o)	7(44°/o)
Grp II(26)	5(19°/o)	9(35°/o)	12(46°/o)
	MAX HR	MAX BP	METS
Grp I(16)	134	168/91	7.5
Grp II(26)	135	165/91	6.0

\* Inadequate

In conclusion, no correlation was found between initial PCW and 3 mos GXT results except for significantly higher maximal exercise level ( $p < .05$ ) attained in pts with PCW < 12mm Hg. (Grp I). The great majority of pts with PCW > 12mm Hg. in the first AMI will have anterior location. Inferior location will be found in most pts with PCW < 12mm Hg. Mean CPK is not significantly higher ( $p > .05$ ) in pts with PCW > 12mm Hg. during their first AMI.

## ABNORMAL HISTOCETIN PLATELET AGGREGATION IN MULTIPLE MYELOMA

Antonio Aponte-Gracia, MD, Francisco Muñiz, MD, San Juan City Hospital, San Juan, Puerto Rico.

Five patients with previously untreated multiple myeloma or in relapse, were studied to determine the incidence of alterations of hemostasis, with special attention to abnormal platelet aggregation. Four of them showed no aggregation with ristocetin and epinephrine, and decreased aggregation with ADP and collagen. Apparently, this abnormal ristocetin-induced platelet aggregation in multiple myeloma has never been reported in the literature, except in association with acquired Von Willebrand's disease. It has been suggested that IgG type antibodies with an apparent specificity for a platelet surface membrane glycoprotein may block ristocetin induced aggregation of normal platelets. If this hypothesis is proven, it could explain our finding in our patients. The inability of patients with multiple myeloma of normal aggregation with ristocetin must be added to the list of hemostasis abnormalities in this disorder.

## THE OBSCURING OF A SECUNDUM ATRIAL SEPTAL DEFECT BY PROLAPSING OF THE MITRAL LEAFLETS

Pablo I. Altieri, MD, Pablo Guzmán, MD, Ernesto E. Guerra, PE., Department of Medicine, University of Puerto Rico Medical School.

The association of prolapsing of the mitral leaflets (PML) with atrial septal defect (ASD) is a well known fact, but the obscuring of an ASD by PML is not.

We studied 81 patients (P) with ASD, 9 P with PML were found. The 9 P. showed unusual auscultatory findings causing that is none of the 9 P, the presence of an ASD was suspected. All 9 P. showed holocystolic murmurs and 6 failed to show fixed splitting of the second heart sound. None of the pure ASD showed left atrial enlargement (LAE) or left ventricular enlargement (LVE). 4 P with PML had LAE and 3 LVE.

The electrocardiograms in all showed right bundle branch block except 4 P with PML who also had first degree A-V block. There were significant hemodynamic differences between the 2 groups in pulmonary arterial pressure (35 vs 17 mm Hg)  $P < 0.2$  and

total pulmonary resistance (149 vs 410)  $P < .002$ , but no difference in pulmonary wedge pressure, cardiac index or left ventricular end-diastolic pressure.

In conclusion in all P with PML with unusual auscultatory findings the possibility of an ASD should be suspected. The cause of this phenomenon probably is due to changes in compliance of the pulmonary artery.

## EXERCISE TREADMILL TESTING IN THE EARLY AND CONVALESCENT PERIOD AFTER ACUTE MYOCARDIAL INFARCTION

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The purpose of this study was to objectively assess by means of treadmill testing (GXT) the estimated functional capacity early after acute myocardial infarction (AMI). GXT was done at 3, 6 and 12 weeks (wks) after documented AMI in 64 patients (pts) without heart failure or unstable angina at the time of testing. Three, 6 and 12 wks GXTs were limited by symptoms, signs (arrhythmia or abnormal blood pressure response) or attaining pre-established end-points (PEEP). PEEP were 4 METS (M) or 70 percent age predicted maximal heart rate (APMHR), 6M or 80 percent APMHR, and 85-90 percent APMHR, 3, 6 and 12 wks GXT, respectively. The mean age for the 64 pts was 55, range 41 to 67. AMIs were transmural in 55 pts (anterior 26, inferior 29) and subendocardial in 9. Twenty-one of 53 3 wks GXTs, 24/57 6 wks GXTs and 49/65 12 wks GXTs were symptoms or sign limited. PEEP was attained in 32/53 3 wks GXTs, 33/57 6 wks GXTs and 16/65 12 wks GXTs. Mean estimated oxygen consumption in symptoms or sign limited GXT at 3, 6 and 12 wks, respectively, was  $2.9M \pm 0.16$  SEM,  $4.7M \pm 0.24$  SEM ( $p < .001$ ), and  $7M \pm 0.24$  SEM ( $p < .001$ ). Forty-four of 175 (23 percent) GXTs had ischemic ST electrocardiographic response during the GXT. There were no com-

plications. In conclusion, GXT at 3, 6 and 12 wks after AMI will demonstrate that 40 percent, 42 percent and 75 percent, respectively of the tests are symptom or sign limited. As a group, symptoms or sign limited pts will show progressive improvement in their estimated cardiac functional capacity at 3, 6 and 12 wks which was statistically significant.

## ASSESSMENT OF PARATHYROID FUNCTION FOLLOWING RENAL TRANSPLANTATION

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Secondary hyperparathyroidism is a universal complication of chronic hemodialysis patients and improves after successful return of renal function following transplantation. Few transplanted patients (T) develop hypercalcemia (HC) or clinical sequelae of hyperparathyroidism despite a well functioning graft and phosphate control, suggesting a severe hyperplastic gland not suppressible at physiologic calcium levels in this group. In order to delineate the natural course of parathyroid recovery we examined maximal serum calcium levels (Ga) in a group of 6 T with functional grafts, before, following transplantation and for periods ranging from 9 to 15 months.

Before transplantation 4 patients had Ca of more than 10.5 mg/dl. During the months of transplant 3 HC showed a fall in Ca while 1 normocalcemic (NC) rose to HC levels, 1 HC became NC. All but one HC and one NC showed intermittent HC that persisted for 1 to 12 months after T. By the 12 months post transplant all T had normal Ca. During this period no patient had any deterioration of renal function related to HC. Metabolic bone survey showed no progressive osteodystrophy. We conclude that our transplanted patients show persistence of HC after successful grafting that represented a delayed in the usual recovery of parathyroid function. Eventual normalization of parathyroid function was the rule in the absence of any ontoward effect or need of parathyroi-



dectomy.

## DURATION OF ACTION OF AN ANTACID IN TWO GROUPS OF PATIENTS

Luis González, MD, Angel Olazábal, (Member), Department of Medicine, Veterans Administration Hospital and UPR School of Medicine, San Juan, Puerto Rico.

Gastric emptying is faster after a truncal vagotomy and pyloroplasty (V + P). We evaluated the duration of action of Maalox ® in peptic ulcer disease (PUD) subjects who had a V+P or were unoperated. Candidates for the study were patients who: 1) had a history of PUD; 2) had a V+P or no gastric surgery; 3) had an UGI x-ray in the previous month showing no delay of gastric emptying; 4) gave written informed consent. After an overnight fast a nasogastric tube was passed and the pH of the gastric contents measured for an hour. 30ml of the antacid was then given and the gastric pH measured for another hour. The duration of action of the antacid was the time the gastric pH stayed above the control pH.

Subjects	Control Gastric pH ( $\bar{x} \pm \text{SEM}$ )	Mean Duration of Action (range)
PUD(N=10)	1.77 $\pm$ 0.12	43(10 - 60) min <sup>△</sup>
V+P (N=6)	3.39 $\pm$ 0.96*	45(5 - 60) min <sup>○</sup>

\* p < 0.01

○ Bilirubin in gastric samples of 5 patients tested.

△ Bilirubin in gastric samples of 4 of 5 patients tested.

In 50 percent of the patients of each group, the neutralizing activity of the antacid had disappeared in 30 min. or less after the dose of antacid. We conclude that: 1) fasting gastric pH is higher in PUD patients with V±P; 2) reflux of duodenal contents occurs frequently in both groups; 3) the duration of action of antacids is not altered by V±P; 4) no antacid effect after 30 minutes is common.

## INCREASED PHARYNGEAL BACTERIAL COLONIZATION DURING VIRAL ILLNESS

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Pharyngeal colonization by gram-negative bacilli (GNB) of normal subjects ranges from 2 to 18 percent. The pharyngeal flora of 89 medical house staff (HS) members was studied longitudinally over an 11 month period, with weekly, biweekly or monthly quantitative oropharyngeal cultures using a 10 cc saline gargle. Twenty percent of the HS studied had one or more GNB in their pharynx during the period of the study.. Colonization by *S. aureus* was 8-9 percent; there was no difference in colonization between sexes, smoking habits or dental hygiene. Colonization was transient and lasted for 2-3 weeks. The most frequent GNB isolated was *K. pneumoniae* and the Klebsiella Enterobacter group accounted for 66 percent of the isolates. Quantitation revealed that 83 percent had > 10 CFU/ml and 44 percent had > 100 CFU/ ml. Colonization by GNB and SA was higher during a presumed viral respiratory illness (66 percent) than during an illness free period (20 percent) for the same subjects. High number of bacteria > 100 CFU/ml was associated with presumed viral URI. The data suggest that pharyngeal colonization of normal individuals by GNB and SA increases during an episode of presumed viral respiratory illness.

## FAMILIAL IDIOPATHIC HYPOPARATHYROIDISM (CASE PRESENTATION)

Melba Feliciano, MD, Manuel Paniagua, MD, Luis F. Castillo, MD - San Juan City Hospital, San Juan, Puerto Rico.

Familial hypoparathyroidism appears to be a rare entity with very few cases reported in the literature. In this study a family is described in which two sisters

developed idiopathic hypoparathyroidism when 4 1/2 and 6 1/2 years old. They presented the condition and other diseases previously described in association with the syndrome such as superficial moniliasis, thyroiditis, adrenal insufficiency, cataracts and gastroparietal cell disfunction. Two cases are presented and the literature revised for a better appreciation of the condition as a result of analysis of clinical features. This is the seventeenth family reported with the condition. The demonstration of serum autoantibodies to endocrine glands as thyroid and adrenal suggests an inherited abnormality in the immunologic mechanism accounting for all these findings.

## HEART RATE IN NORMAL PUERTORICAN CHILDREN

Francisco Torres Aybar, MD, FACP, Miguel Rivera Torres, MD and Diego Alcalá Ocasio, MD

Judgment of normal growth and development in our pediatric population is usually based on standards established in other countries. The same pattern holds for normal pediatric electrocardiographic values in our children. A study conducted at the Department of Pediatrics of the Ponce District Hospital included 790 normal children. All the individuals were carefully evaluated from the cardiovascular point of view by means of a thorough physical examination, electrocardiogram and chest radiography. All electrocardiograms were performed by one of us under basal conditions and in absence of any acute illness. The heart rate was measured from these electrocardiograms (utilizing lead 2 for this purpose) from birth to 15 years of age as a whole group and also considering sex. Mean values and standard deviations were also calculated separating both sexes and as a whole group. These results are just the beginning of a more ambitious study that will determine the normal electrocardiographic values for our pediatric population.

## PREVALENCE OF HUMAN SCHISTOSOMIA-

## SIS MANSONI IN PUERTO RICO: A LIMITED PREVALENCE STUDY

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One hundred and ninety five serum samples (82 males, 114 females) were obtained at the Annual Health Fair held in the San Juan Coliseum in 1977. The serum samples were obtained from individuals living in 19 cities and towns, although the majority came from 4 areas near metropolitan San Juan (Río Piedras, San Juan, Carolina, and Bayamón). All of the serum samples were tested two or more times for antibodies to fresh *Schistosoma mansoni* eggs by the circumoval precipitin (COP) test. The COP test was used because it has been shown to have the greatest diagnostic sensitivity and specificity of 9 serologic tests used for the serodiagnosis of schistosomiasis and has been more accurate in detecting infections than a single, sensitive stool examination. Thus, results with the COP test, properly done, could serve as a useful tool in seroepidemiological studies for the prevalence of schistosomiasis. Of all serum samples tested, 13.8 percent were positive by the COP test (14.6 percent males, 13.2 percent females). Most (92.6 percent) of the reactions were blebs, suggesting low levels antibody and probably lightly infected individuals. We were surprised to observe that of 116 samples collected from residents in San Juan and Río Piedras, 19 (=16.4 percent) were positive by the COP test. These results suggest that the prevalence of schistosomiasis mansoni in Puerto Rico may be higher than present estimates and warrant a more thorough island-wide survey by the local health authorities.

## COMPARISON OF AMBULATORY AND INPATIENT EVALUATION OF RECURRENT CALCIUM STONE SUBJECTS IN P. R.

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vices, VA Hospital, San Juan, Puerto Rico.

Four hundred and sixty (460) recurrent stone formers (S) have been evaluated on ambulatory basis. In order to establish the relationship between a practical ambulatory and a more controlled hospital evaluation a group of 12 S and 8 controls (C) were admitted and evaluated while on regulated diets of 400 mg, 800 mg, 1200 mg calcium (Ca). Results were compared with values obtained in the evaluation of both S and C while on a random regular outpatient Puertorrican diet with an estimated Ca content of 800 mg. Cumulative daily urinary excretion of Ca (UCa) was as follows in mg/24 hrs. ( $\bar{x} \pm SE$ )

Ca Intake	400 mg	800 mg
S (n = 12)	181 $\pm$ 4	207 $\pm$ 13
C (n = 8)	104 $\pm$ 4	141 $\pm$ 5
Ca Intake	1200 mg	Random
S (n = 12)	211 $\pm$ 8	192 $\pm$ 16
C (n = 8)	160 $\pm$ 5	159 $\pm$ 9

There was a significant difference among S and C in most daily UCa determinations in center and ambulatory. When these determinations were compared with the 800 mg Ca intake consistent with a regular P. R. diet there was no significant difference. A separate analyses of UCa by S and C showed an overlap between UCa observed during 800 mg and 1200 mg intake but not at 400 mg. A subgroup was identified with abnormal significant UCa observed at all levels of Ca intake. In conclusion: On the basis of the center studies we can define abnormal calcium excretion in S in the absence of hypercalciuria at most levels of Ca intake. Discrimination is best at the 400 mg Ca although hypercalciurics could be identified of all levels of intake if compared with matched controls.

## TOXOPLASMA ANTIBODIES IN CHRONIC RENAL PATIENTS

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Chronic renal patients (PTS) are immunosuppressed subjects that frequently develop fever with an unclear etiology. A titer  $> 256$  of toxoplasma antibodies is considered a sign of active infection. A study was designed to determine the toxoplasma antibodies in a group of 95 PTS with chronic renal disease and to compare these antibodies to a control population. Male VA PTS on chronic hemodialysis were utilized and serial toxoplasma antibodies determined by the indirect fluorescent antibody technique. Forty percent (38/95) showed negative titers, 3/95 titers 1:16, 21/95 titers 1:64, 19/95 titers 1:256 and 14/95 titers  $> 1:1024$ . Of the 57 subjects with positive titers, 33 had serial determinations and in 8/33, the titers rose while in 7/33 the titers decreased. When compared to a randomly selected Puerto Rican population (control), it was found that 62 percent of the male control group and 60 percent of the studied subjects had positive titers. In the control group 9/31 or 29 percent had titers  $\geq 1:256$ , in the studied subjects it was 35 percent (33/95). Of significance is that 14/95 or 14.7 percent of studied subjects had titers of 1:1024 or greater while only 1/31 or 0.3 percent of the controls. The percentage of chronic hemodialysis PTS with toxoplasma antibody titers  $\geq 1024$  is higher than in the controls. The significance of an isolated toxoplasma antibody titer of  $\geq 1:1024$  in an asymptomatic chronic hemodialysis PT is unclear; it may be a reflection of alterations in cell mediated immunity or persistence of antibody and humoral immunity. In a chronic hemodialysis PT with high toxoplasma titers and fever, or with serially increasing titers consideration for treatment should be given.

## CENTRAL NERVOUS SYSTEM MANIFESTATIONS IN SYSTEMIC LUPUS ERYTHEMATOSUS

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Central Nervous System (CNS) in systemic lupus erythematosus (SLE) is not uncommon. It has been reported to occur in 21 to 75 percent of the cases.

Sixty three patients with SLE who developed CNS manifestations were studied. There were 54 females and 9 males. Thirteen patients had developed SLE before age 15. Of the 63 patients, 34 patients developed psychosis, 26 convulsions, 9 hemiparesis, and cranial nerve involvement in 6. Twelve patients had more than one neurologic manifestation.

Twenty six patients died. Of this group, 34 percent developed the CNS as presenting symptom. Only 5 patients died with acute cerebritis. The rest died of other complications.

Twenty three patients had CNS manifestation and no kidney or heart involvement. Of this group 5 died. Nineteen patients had CNS, heart and kidney involvement, of this group 16 patients died.

Mortality was higher among patients with psychosis and those with heart, kidney and CNS involvement.

## DIFFERENTIAL DIAGNOSIS OF SHOULDER LESIONS

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The author has observed signs in the shoulder region that have assisted him in the diagnosis of shoulder-girdle versus shoulder joint lesions. These consist of: 1. Limitation of scapular motion in shoulder girdle lesions, 2. Reduction of joint motion with intraarticular pathology, 3. Changes in the pattern of rotation of the shoulder joint with intraarticular problems, and 4. Determining the anatomical site of the tear by localizing the superior segment of the shoulder capsule.

Except for a variation of number 4, these signs have not been reported by others in the medical literature.

## WHAT ACHES THE ADOLESCENT? WHAT

## SHOULD WE DO?

*José Ramírez Rivera, FACP, Angel Rafael Braña, MD, Edisson H. Osorio, MD - Rincón Rural Health Initiative Project, Rincón, Puerto Rico.*

Twenty three percent of the population in Rincón are adolescents. In February, 1978, 500 students between seventh grade and fourth year high school answered a questionnaire designed to obtain an accurate idea of their health needs. Ninety eight percent feel their nutrition is adequate. Eighty five percent feel they are reprimanded or punished by their parents and teachers frequently and unnecessarily. Five percent use alcohol occasionally or frequently. Five percent use marihuana, heroin or other drugs to some extent. Fifty one percent feel partially or totally unsatisfied with themselves. Ninety one percent feel bored, and complain the lack of recreational activities as the biggest problem. Thirty one percent have thought of committing suicide at least once. Fifty six percent have acne. As a result of these observations we have developed a psychosocial unit staffed by a Social Worker, Registered Nurse, Nutritionist, Coordinator of Activities, Counselor, and Psychologist. They have observed that twenty percent of their adolescent clients were obese; 22 percent were underweight and 37 percent filled other criteria to participate in the WIC Program. Eighty percent suffered from disturbed family dynamics and fifty percent had difficulty in relating to their peers. Fifty percent had learning disabilities. Thirty five percent needed general medical treatment. Twenty five percent needed specialized dermatologic care.

The importance of a separate unit for the health maintenance of the adolescent will be demonstrated.

## BONE SCANNING IN PATIENTS WITH CARCINOMA OF THE CERVIX

*Samuel Sostre, FACP and Mohammed Kazmain Zaidi, MS-University of Puerto Rico*

Whole body bone scans were performed on 34

patients with cervical carcinomas to evaluate the usefulness of the procedure in the detection of bony, urinary tract and soft tissue abnormalities in this disease.

Patients of all four stages were included in the study. The bone scan was performed when recurrence of disease was suspected after treatment, or when widespread disease was suspected on the initial evaluation. All the patients had intravenous pyelograms (IVP) and BUN determinations. All patients with scintigraphic bone abnormalities or with osseous symptoms also had roentgenographic skeletal surveys.

Six patients (14.7 percent) were correctly diagnosed to have metastatic bone disease by bone scanning. No false negative studies were found. The bone scan correctly identified 14 urinary tract abnormalities in 12 patients (12/34-35 percent). These included 6 non functioning kidneys, 4 obstructed kidneys, 2 patients with renal ptosis, and 2 with bladder compression due to pelvic masses. The bone scan missed only 1 case with urinary tract obstruction. This performance is comparable to the IVP which also missed 1 case of UT obstruction in this series. In addition, the bone scan correctly identified five other miscellaneous conditions (which included lymphedema, bone fractures and avascular necrosis of the femoral head) for an overall detection rate of 25 abnormalities in 34 patients.

Bone scanning is a very useful tool in the evaluation of the patient with advanced carcinoma of the cervix. It not only detects metastases to bone very early, but also aids in the identification of urinary tract abnormalities and in the detection of other non neoplastic bone disease and soft tissue abnormalities.

## PROTON BEAM TREATMENT OF PITUITARY DISEASE: UNIVERSITY HOSPITAL EXPERIENCE

*Francisco Aguiló Jr., MD, FACP, Department of Medicine and Clinical Research Center UPR School of Medicine, San Juan, Puerto Rico.*

During the past 3 years we have submitted 7 patients to proton beam irradiation (given at the Harvard, Mass. Cyclotron), for the following diagnoses:

4 Cushing's syndrome, 1 acromegalic and 2 prolactinomas, trying to achieve control of the disease by effective non-invasive means.

There were 5 females and 2 males. Age ranged from 23 to 57 years. All were evaluated pre and post-irradiation at our institution. Dose ranged from 4,500 to 11,000 rads.

Two patients with Cushing's were cured in less than one year; their residual pituitary function was normal. A patient with primary amenorrhea improved, with normalization of prolactin levels. The acromegalic patient improved within 2 years but is not yet cured.

In 3 patients their disease became worse following irradiation: metabolic parameters of activity increase 10-50 percent in the acromegalic; a Cushing's patient had further increase in hypercorticism and hypertension, and died from a heart attack; and a young male with prolactinoma having suprasellar extension had to undergo hypophysectomy 3 months post proton beam due to progressive visual field loss. Another Cushing's (unresponsive to dexamethasone) developed unilateral ptosis and diplopia; she was submitted to total adrenalectomy 1 year later.

Our short experience calls for close follow-up and careful monitoring after proton beam irradiation.

## TOXOPLASMOSIS SEROLOGIC SURVEY OF 100 SUBJECTS IN PUERTO RICO: A PILOT STUDY

*H. Gorbea, MD, M. Medina, MS and C. H. Ramírez-Ronda, FACP - Laboratory and Research Service, VAH, Depts. of Medicine, Pathology and Microbiology, UPR School of Medicine, San Juan, Puerto Rico .*

Toxoplasmosis (T) is a common disease occurring in animals and man throughout the world. An estimated 25 percent of the adults in the U. S. have antibodies indicating infection at some time in their life and are presumed to be immune to further infection. In Puerto Rico a serologic study performed in 1972 revealed that 51 percent of women of child-bearing age and 8 percent of the children had antibodies against *Toxoplasma gondii*. A study was designed to determine antibodies in a group of 100 sub-

jects divided into 4 age groups, ages 10-20, 21-30, 31-40, 41-50, 51-60 and compare the serologic titers between groups and between sexes. Serum samples were taken from our serum bank, obtained from normal patients in the San Juan Metropolitan area. Toxoplasma antibodies were determined by the indirect fluorescent antibody test (IFA). The percent of subjects with positive T antibodies increased with age from 30 percent in the males, age 10-20, to 90 percent in the males, age 51-60. 80 percent of the females in the age 51-60 were found positive. Over 50 percent of the adults studied were found positive; 29 percent of the males and 10 percent of the females had titers >256. There was a uniform distribution of titers among the studied groups. The percent of subjects with positive titers for T antibodies in Puerto Rico is higher than in U. S. A. Males and females with positive T antibodies is similar (62 percent and 54 percent), the number of males with titers > 256 was higher. Low titers indicate immunity but very high titers indicate a recent infection which may require treatment. A larger serologic survey should be carried out in Puerto Rico.

## NEPHROGENOUS CYCLIC AMP IN THE EVALUATION OF RECURRENT CALCIUM STONE FORMERS

*L. Lespier-Dexter, (Member), F. Burgos, (Member) - Research and Medical Services, VA Hospital, San Juan, Puerto Rico.*

We have established the method of nephrogenous cyclic AMP (NcAMP) as a measure of parathyroid function in the evaluation of a number of abnormalities in calcium metabolism such as hyperparathyroidism (HPT), pseudohypoparathyroidism (PHP), hypoparathyroidism (HPO) and for the follow up of surgically parathyroidectomized subjects. In order to establish parathyroid function in S and classify them in sub-groups we performed 45 determinations of NcAMP in 8, S, 4 HPT, 2 HPO, 3 PHP and 19 controls (C). Analysis of the data showed, NcAMP (n moles/100 ml GFR) in HPT of  $6.36 \pm 6.30$  significantly higher ( $p < 0.005$ ) than in S;  $2.80 \pm 1.07$ . S value was comparable to controls;  $3.02 \pm 1.35$  and PHP;  $2.93 \pm 1.49$ .

S values was significantly higher ( $p < 0.001$ ) than HPO:  $0.12 \pm 0.35$ . When each S was individually plotted and compared, we could differentiate S with definitely increase in NcAMP ( $n=2$ ) in the absence of hypercalcaemia. One had documented elevation in parathyroid hormone (PTH). Most of S had values that fell within the normal range and a group of S, ( $n=2$ ) had depressed values. In conclusion measurement of NcAMP permitted us to differentiate the groups of recurrent calcium stone formers; group with a renal leak with negative chronic calcium balance hypercalciuria, secondary elevation in parathyroid function and thus increase in NcAMP. A second group represents those with a hyperabsorptive state, depressed parathyroid function and NcAMP. A third group represents those with normocalciuric nephrolithiasis whose mechanism of disease is only related in part to an abnormality in calcium handling. This has therapeutic implications.

## CARDIAC ISOENZYMES IN ACUTE MYOCARDIAL INFARCTION

*Velia Toledo, MD (Associate), Jorge B. Morales, MD and Félix M. Cortés, MD, FACP*

Isoenzymes of Creatine Phosphokinase (CPK) and Lactic Dehydrogenase (LDH) were studied in 60 patients with acute onset of chest pain admitted to the Coronary Care Unit. Results of serial Isoenzymes were correlated with the Electrocardiographic Diagnosis of Acute Myocardial Infarction. (A.M.I.) According to the results these patients could be classified into 5 different groups:

Group I: 26 patients with no evidence of Acute Myocardial Infarction by the EKG or isoenzyme studies.

Group II: 16 patients with classic EKG and Isoenzyme patterns of Acute Myocardial Infarction.

Group III: 12 patients with complete BBB and Neg. EKG for A.M.I. Of 9 with complete LBBB, 4 had Isoenzyme patterns of A.M.I. complete RBBB was present in 3 cases - all with normal Isoenzymes.



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# The Maker

## Examining a Few Myths About Prescribing.

Increasing pressure is being put on the practicing physician to prescribe drugs generically. You are told that brand-name products are universally "expensive" and generic versions are relatively "cheap." To make this case, the most extreme (rather than typical) price differentials are cited. Thus, consumers are led to believe that such differentials are commonplace. Even your knowledge and your motives as a physician are questioned.

Understandably, these views have created myths. We think it's time to examine them in the light of all the facts and ramifications.

*MYTH: There are no differences in quality and performance between brand-name products and their generic counterparts. The corollary is that there are no differences among products made by high-technology, quality-conscious, research-based companies and those made by commodity-type suppliers.*

**FACT:** The Food and Drug Administration does a good job in monitoring a generally excellent drug supply. Still, it has nowhere near the resources to guarantee the quality and bioavailability of all marketed products at any given time. Just a few months ago, for example, it noted that batches of tetracycline HCl capsules which met official monograph requirements were

not bioequivalent to a reference product. As you know, there is substantial literature on this subject affecting many drugs, including such antibiotics as tetracycline and erythromycin. The record of drug recalls and court actions affirms strongly that there are differences among pharmaceutical companies and their products. Research-intensive companies have far better records than those that do no research and may practice minimum quality assurance.

*MYTH: Industry favors only "expensive" brand names and denigrates all generics.*

**FACT:** PMA companies make 90 to 95 percent of the drug supply, including, therefore, most of the generics. Drug nomenclature is not the important point; it's the competence of the manufacturer and the integrity of the product that count.



# Matters.

**MYTH:** Generic options almost always exist.

**FACT:** About 55 percent of prescription drug expenditure is for single-source drugs. This means, of course, that for only 45 percent of such expenditure, is a generic prescribing option available.

**MYTH:** Generic prescriptions are filled with inexpensive generics, thus saving consumers large sums of money.

**FACT:** Market data show that you invariably prescribe—and pharmacists dispense—both brand and generically labeled products from known and trusted sources, in the best interest of patients. In most cases the patient receives a proven brand product. Savings from voluntary or mandated generic prescribing are grossly exaggerated.

**MYTH:** Drugs account for a major portion of the rise in health care costs.

**FACT:** Drugs represent a very small part of such costs. The amount of the health care dollar spent for prescription drugs was about 12 cents in 1967; today it is about 8 cents. And you as a physician are most conscious of how drug therapy can cut hospitalization, avert surgery, reduce office visits and keep patients on the job.

**MYTH:** Government intrusions into the marketplace will save tax money.

**FACT:** Government schemes always cost the taxpayer something, and the costs often exceed the benefits. Certainly, any federal “help,” such as lists of wholesale drug prices sent to all physicians and pharmacists, will be no exception. Just think of the expense of keeping them current! Moreover, wholesale prices are poor guides to actual transaction prices and even worse guides to retail prices.

## The PMA Position

We believe your freedom to prescribe, either by generic or brand name, should be totally unabridged. Otherwise, your prescribing prerogatives and your relationships with patients will be seriously impaired.

## The maker does matter

After the myths about price and equivalency have been shattered, one fact stands out more clearly than ever: *The maker does matter.* As always, your best guide to drug therapy for your patients is to select products—both brands and generics—from manufacturers with credentials and performance records you have come to respect.



Pharmaceutical Manufacturers Association  
1155 Fifteenth Street, N.W.  
Washington, D.C. 20005



## AVISO DE INTERES

La Junta Editora, consciente de su responsabilidad de hacer que el "Boletín" cumpla a cabalidad con su cometido de divulgar conocimientos médicos, elevar las normas de educación médica y al propio tiempo de llenar las necesidades de todos los compañeros médicos, ha acordado establecer una nueva Sección que se conocerá como "Sección de Preguntas".

Bajo esta nueva Sección, todos los compañeros tendrán la oportunidad de enviarnos preguntas médicas de casos difíciles o casos clínicos para opinión experta. Estas preguntas, con sus respuestas, serán publicadas en esta nueva Sección.

Las preguntas deberán ser enviadas a:

Boletín de la AMPR  
Sección de Preguntas  
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Esperamos sus preguntas.

Juan M. Aranda, MD  
Presidente  
Junta Editora

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**CONTRAINDICATIONS:** Because of the quinine content, Quinamm is contraindicated in women of childbearing potential, in pregnancy, in patients with known quinine sensitivity, and in patients with glucose-6-phosphate dehydrogenase deficiency. Hemolysis (with the potential for hemolytic anemia) has been associated with a G-6-PD deficiency in patients taking quinine.

**PRECAUTIONS:** Thrombocytopenic purpura may follow the administration of quinine in highly sensitive patients. Recovery will follow withdrawal of the medication. Cinchona alkaloids, including quinine, have the potential to depress the hepatic enzyme system that synthesizes the vitamin K-dependent factors. The resulting hypoprothrombinemic effect may enhance the action of warfarin and other oral anticoagulants.

**ADVERSE REACTIONS:** Aminophylline may produce intestinal cramps in some instances, and quinine may produce symptoms of cinchonism, such as tinnitus, dizziness, and gastrointestinal disturbance. If ringing in the ears, deafness, skin rash, or visual disturbances occur, the drug should be discontinued.

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1 tablet upon retiring. When necessary, 1 additional tablet may be taken following the evening meal.

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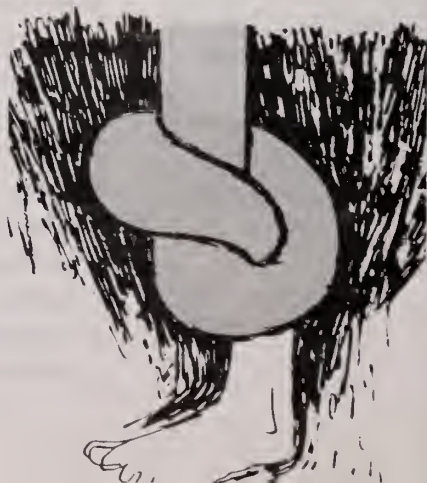
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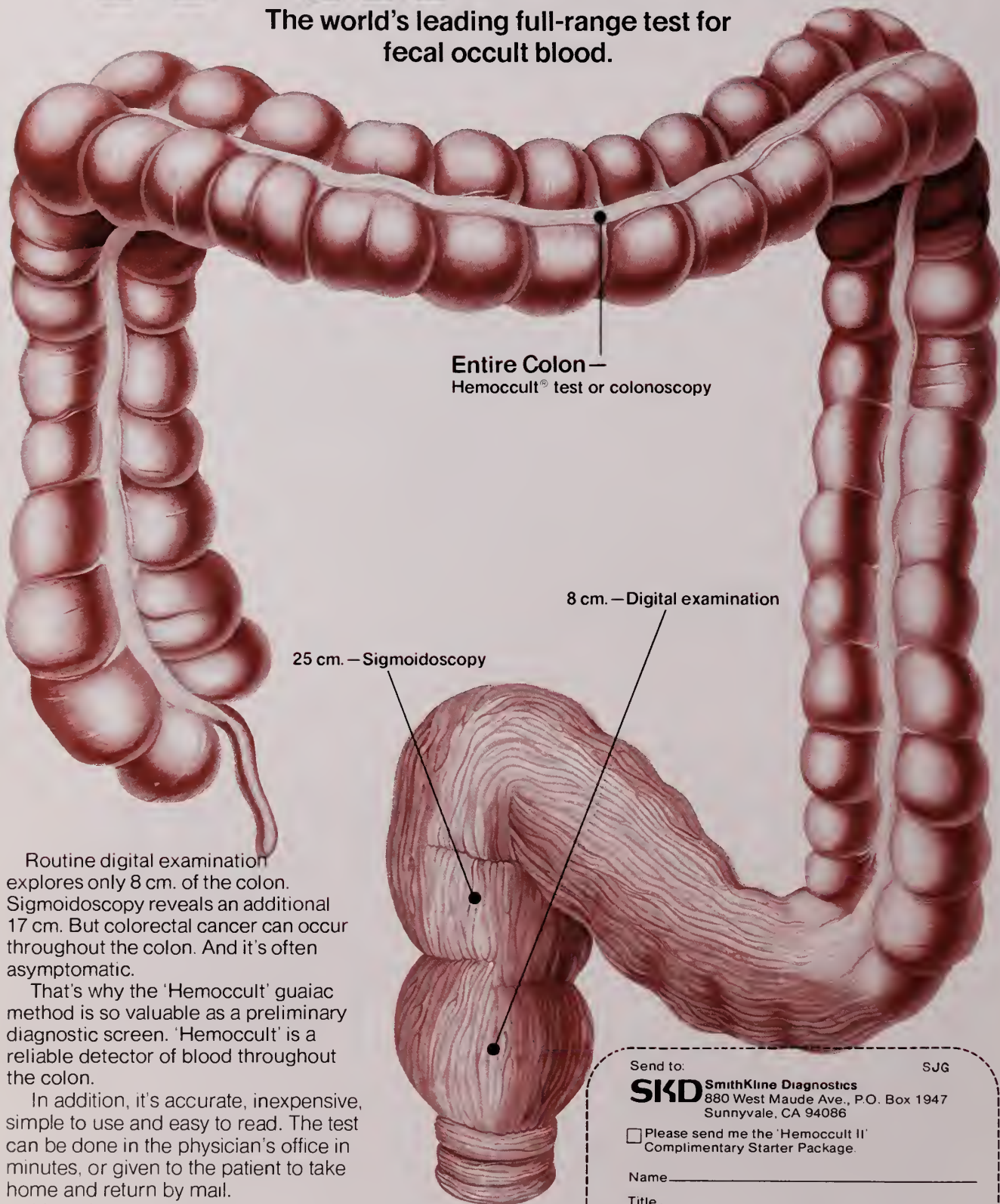
Nocturnal recumbency leg muscle cramping is frequently an unwelcome bedfellow for many patients—especially those with arthritis, diabetes or peripheral vascular disease ... consider Quinamm ... simple, convenient dosage—usually just one tablet at bedtime ... can provide restful, welcome sleep without night leg cramps.

See opposite page for prescribing information.



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Group IV: 3 patients with dissociation of Isoenzymes and non diagnostic EKG findings - Probably A.M.I. in spite of non diagnostic EKG.

Group V: 3 patients with Ischemic T - Wave changes in the EKG and no evidence of A.M.I. by Isoenzyme studies.

Conclusion: Serial Isoenzyme studies correlate well with EKG Diagnosis of Acute Myocardial Infarction. In some patients Isoenzymes patterns may be diagnostic of A.M.I. even when the EKG is not diagnostic. Representative cases will be presented.

## **PROSPECTIVE STUDY OF PENICILLIN SKIN TEST IN AN INPATIENT POPULATION**

*Edwin Meléndez Ríos (Associate), José N. Moreno, MD (Member) San Juan City Hospital, San Juan, Puerto Rico.*

A prospective study of penicillin skin test in an inpatient population was performed at the Department of Medicine of the San Juan City Hospital.

The population studied was divided into 2 groups. Group I consisted of 34 patients with history of penicillin allergy of which 16 patients required penicillin therapy. The patient were skin tested with Pen G and Pre-pen (major determinant). 21 patients (62 percent) had negative skin test. Of the sixteen patients which required penicillin therapy 11 (69 percent) had negative skin test. Eight of these 11 patients (72 percent) received penicillin without any adverse effect. The other 3 received cephalosporin without any adverse effect.

Group II consisted of 27 patients without a history of penicillin allergy which required penicillin therapy. They were skin tested with Pen G and Pre-pen. 2 out of 27 (7 percent) patients had positive skin test and they were treated with an alternate drug (Clendamyacin; Cephalosporin) 25/27 had negative skin test and received penicillin without any adverse effect.

In conclusion in our hands properly performed penicillin skin test allow us to give penicillin in 69 percent of patients with a past history of penicillin

allergy without any adverse reaction. Even more important penicillin skin test allow us to identify 7 percent of patients without any history of penicillin allergy, which would have been at a greater risk of developing an allergic reaction, which could'nt been identified on the basis of the history alone.

## **TWO DOSE SCHEDULES OF GOLD IN RHEUMATOID ARTHRITIS**

*René A. Hernández, MD, Raúl Zambrana, MD - Department of Medicine, San Juan City Hospital, San Juan, Puerto Rico.*

A trial of two dose schedules of gold salts administered to patients with definitive or classical rheumatoid arthritis was performed in a prospective, double-blind study for 20 weeks period. The purpose was to ascertain whether small dose are as effective as conventional doses. Six patients in the lower dose group with active disease of greater than two months were given 15 mg. of gold salt weekly for twenty weeks. Six patients in the standard dose group received 50 mg of gold weekly for the same period. No patient received concomitant steroid or antimalarial therapy. No statistical differences were observed in the rheumatoid activity index of the two groups. The only difference of significant value was in the joint count that was greater in the standard dose group. Three patients of the low dose group and one of the standard dose were withdrawn because of drug toxicity.

The data indicate that 15 mg of gold per week is as effective as 50 mg when administered as described above.

## **AORTIC STENOSIS, NON INVASIVE INDEXES OF SEVERITY**

*Marylin Ríos, MD (Associate), Ralph Conaway, MD, José Fernández Martínez, MD, FACP, FACC, José Pérez Hernández, MD and José A. Serrano Muñoz, MD, FACC - San Juan City Hospital, San Juan, P. R.*

Echocardiography and systolic time intervals have both been used for the evaluation of the severity of aortic stenosis but the results have not been compared. Previous reports have found a good correlation between the left ventricular systolic pressure found during cardiac catheterization and the echocardiographic formula:  $LVSP = LVSD/LVST \times 225$ , where LVSP is the ventricular systolic pressure, LVSD is the ventricular systolic diameter, LVST is the systolic endocardial thickening as found by echocardiogram,

and 225 is an empirical constant. By subtracting the systolic pressure found by an arm cuff, from this figure the aortic gradient can be estimated.

In this report both systolic time intervals and echocardiography are used to evaluate seven patients with aortic stenosis and these results are compared with cardiac catheterization results.

A prolonged LVET, U time, T time and  $Q S_2$  were found to be far better parameters of severity than the echocardiographic gradient estimation.

### MEDI-QUIZ para Cardiólogos — Agentes Antiarrítmicos

- |                 |  |
|-----------------|--|
| 1. Quinidina    | A. Disminuye la depolarización en la fase A del potencial de acción (disminuye automaticidad). |
| 2. Procainamida | B. Disminuye la velocidad de la fase O del potencial de acción (disminuye conducción).         |
| 3. Disopyramida | C. Aumenta la velocidad de la fase O del potencial de acción (aumenta conducción).             |
| 4. Inderal      | D. Alkaloide rawvolfia de uso intravenoso.   |
| 5. Lidocaina    | E. Inhibe corrientes lentas de $Ca^{++}$ .   |
| 6. Dilantin     | F. Derivado de papaverina, se usa como agente antianginoso.                                    |
| 7. Bretylium    | G. Derivado de fenotiazida, sintetizado en USSR. Efectivo en taquicardia supraventricular.     |
| 8. Ajmaline     | H. Puede interferir con la síntesis de $T_3$ y $T_4$ .   |
| 9. Ethmozin     |  |
| 10. Verapramil  |  |
| 11. Nifedipina  | (Contestaciones en página 383)   |
| 12. Amiodarona  |  |

## NOTICIAS

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### *NEWS from THE AMERICAN ACADEMY OF FAMILY PHYSICIANS*

#### *EXERCISE STRESS TESTS PART OF CLINICAL EXAMS*

Atlanta — A professor from Emory University School of Medicine contends that “exercise stress testing must be considered as an extension of the clinical examination.”

This was the contention of Dr. Nanette K. Wenger, who is also director of Cardiac Clinics, Grady Memorial Hospital, Atlanta, in speaking to family doctors at the Annual Scientific Assembly of the American Academy of Family Physicians (AAFP). The Georgia World Congress Center is the Assembly site.

Dr. Wenger noted that exercise stress testing can be performed to “(1) help establish the diagnosis of coronary atherosclerotic heart disease, (2) evaluate functional capacity in patients with many forms of heart disease. . . and estimate the patient’s performance in daily living, occupational, and recreational situations, (3) write an individualized exercise prescription for exercise training, (4) evaluate the results of the subsequent exercise training, and (5) evaluate the results... of....medical and surgical therapeutic interventions.”

However, there are some inadequacies of the single stage exercise stress test: Dr. Wenger noted that this method may not accrue the desired statistics for a physically fit person, and at the other end of the spectrum, for the seriously impaired patient.

She continued with requirements for stress testing, particularly for the cardiovascular patient. One of the requirements is an on-site physician. This is not only necessary for legal reasons, she stated, “but because there is a major difference between the total information available” to observing the patient and “an exercise electrocardiogram,” which a physician can review after the test is performed.

Dr. Wenger also addressed situations where stress testing is not advised, such as patients with “new or unstable chest pains” and “recent defined myocardial

infarction.”

A graduate of Harvard Medical School, Dr. Wenger is a member of the Board of Directors of the American Heart Association.

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### *FROM THE AMERICAN OCCUPATIONAL MEDICAL ASSOCIATION*

#### *EPIDEMIOLOGY FOR THE OCCUPATIONAL PHYSICIAN -- Postgraduate Seminar to be held.*

Chicago — A postgraduate seminar offering practical concepts and applications in “Epidemiology for the Occupational Physician” will be held Feb. 12 -16, 1980, at the Grenelefe, a Radisson Resort in Cypress Gardens, Fla. The seminar is presented by the American Occupational Medical Association (AOMA) and the National Heart, Lung and Blood Institute.

The four-day seminar is specifically designed for occupational physicians and will offer practical epidemiology concepts and applications. Information to be presented includes:

- \* how to design and carry out an epidemiological study;
- \* measures of disease risk which can be applied to groups;
- \* how screening and detection of occupational disease can be accomplished;
- \* methods of evaluating epidemiological studies;
- \* using epidemiological findings in occupa-



tional standards; and

- \* requirements for an occupational health surveillance system and how such data may be used.

Each major presentation of the seminar will be followed by a small group discussion so that content may be mastered. Early pre-registration is recommended. Space is limited to 40 physicians. A faculty/student ratio of 1 to 7 has been established to aid individual understanding. Experts in epidemiology and biostatistics drawn from academia, industry and government will serve as faculty.

Registration fee for the seminar is \$265.00, which includes a banquet on Tuesday, Feb. 12. The registration fee is exclusive of lodging; Grenelefe registration cards will be sent to registrants by AOMA.

As an organization accredited for Continuing Medical Education, AOMA certifies that this Continuing Medical Education activity meets the criteria for 24 Credit Hours in Category I of the Physicians Recognition Award of the American Medical Association.

For further information about the seminar, write: Don Hoops, PhD, Director of Education, American Occupational Medical Association, 150 North Wacker Drive, Chicago, IL 60606, or call: (312) 782-2166.

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#### AMA NEWS:

#### SEED SPROUTS IN BOY'S EYE IN RARE MEDICAL HAPPENING

Chicago - A highly unusual medical case in which a small seed germinated and began to grow in the eye of an 8-year-old boy is reported in the current issue of an American Medical Association specialty journal.

The report is from Dr. Solomon Abel, an eye specialist in Cape Town, South Africa.

The boy was brought to Dr. Abel after ten weeks

of discomfort in the left eye. Some 18 months earlier he had returned home from school with a swollen left eye for which there was no obvious explanation.

The doctor found a spiraling shoot about one-eighth inch long growing just under the surface of the eyeball. The seed and its sprout were removed under microscopic surgery. The eye healed and vision was unimpaired. Botanists examined the plant and reported that it was a seedling of a dicotyledonous plant of the Compositae family. How it became embedded in the child's eye was not determined.

The report in Archives of Ophthalmology for September says several similar cases are found in medical annals. Dr. Abel points out that conditions essential for germination of seeds include moisture, warmth, fresh air and protection from strong light. Apparently the eyeball provides these conditions.

#### IMMUNE GLOBULIN TREATMENT BRINGS DECLINE IN RH DISEASE

Chicago — Rh hemolytic disease, a serious and often fatal illness of the newborn, has been reduced in the United States in the past ten years, but more efforts are needed to eliminate the disease completely.

A research group from the Center for Disease Control, Atlanta, reports in the September 28 Journal of the American Medical Association that infant deaths from Rh disease decreased from 941 in 1968 to 269 deaths in 1975.

Rh disease is an illness that occurs when a mother who has the Rh-negative factor in her blood gives birth to an Rh-positive infant. The child is seriously ill from the clash of blood factors in the body. The condition can be treated by exchange blood transfusions in the infant, but sometimes it is fatal.

Usually the first pregnancy of the Rh-negative mother causes no serious problem in the infant. But the act of birth, or abortion or miscarriage, sensitizes the mother to the blood factor, and subsequent infants may have serious problems.

The further sensitization may be forestalled by

administering Rh immune globulin to the mother following delivery, or following abortion or miscarriage. This substance has been available since 1968, and its use has grown steadily through the decade.

Rh immune globulin was administered to 80 per cent of eligible Rh-negative women in 1974, and to 82 per cent in 1976.

The researchers point out that in the next decade most women sensitized before Rh immune globulin became available will complete their families, and if it is used effectively "we should observe the virtual disappearance of Rh sensitization and Rh hemolytic disease." This will require an extra effort on the part of the medical community to raise the 82 per cent figure to as near as possible 100 per cent.

The report is by J. William Flynt, Jr., MD and colleagues.

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#### **TREATMENT FOR HODGKIN'S DISEASE CAUSES LOSS OF SEXUAL FUNCTION**

Chicago — Chemical castration is the price of the "cure" of Hodgkin's Disease, says an article in the Oct. 26 Journal of the American Medical Association. And it doesn't have to happen.

For more than 30 years medical science has been able to prolong life and sometimes virtually cure this serious cancer of the lymph nodes. But doctors are only now discovering that the drugs that are used in the treatment often destroy the sexual function of the patient.

The studies are the work of Ramona M. Chapman, MD, and Simon B. Sutcliffe, MD, at St. Bartholomew's Hospital, London. Dr. Chapman is now at Walter Reed Army Medical Center, Washington, and Dr. Sutcliffe is at Princess Margaret Hospital, Toronto.

It is not the disease itself that damages hormone function, says Dr. Chapman. It is the drugs used to treat the disease.

Under the drug treatment, the disease responds well, but "young women show a pattern of progressive ovarian failure accompanied by severe estrogen defi-

ciency and lack of libido. The loss of ovarian function seems to result from the chemotherapy."

The researchers cited many instances of marriage problems and failures and other social ills among women "cured" of Hodgkin's Disease by drug treatment. The reluctance of the patients to talk with their doctors about it caused great anguish and suffering among patients for the past 30 years, she declares. The doctors did not know of the sexual malfunction.

Now that the side effect of the drugs is known, it usually is possible to offset the sexual loss by hormonal replacement, accompanied by appropriate counseling so that the patient will understand that loss of libido is to be expected during drug treatment, and can be corrected by hormones.

In an accompanying editorial, William H. Crosby, MD, of La Jolla, Cal., declares:

"We were unaware that the pulses of drugs used in Hodgkin's Disease destroyed libido, ruining personal relations and disrupting families — this in addition to causing sterility. An unbelievable amount of human misery has been silently borne by the patients of three decades."

Now that the problem is known to doctors and hormonal replacement is available for those receiving drug treatment for Hodgkin's Disease, the response has been gratifying.

"They come in like shrinking violets; we treat them and they come back like English roses."

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#### **GASOLINE SWALLOWING WHILE SIPHONING IS HEALTH HAZARD OF ENERGY CRUNCH**

Chicago — Add to the headaches caused by the national energy shortage — the swallowing of gasoline during the process of siphoning.

With the present gasoline shortage, the incidence of gasoline swallowing by adults has greatly increased, says a report in the Nov. 2 Journal of the American Medical Association.

The Maryland Poison Information Center normally

receives less than one call per day involving accidental swallowing of gasoline, says Dr. Wendy Klein Schwartz, Baltimore. In all of 1978 there were 235 calls. But during the month of June, 1979, with lines at the pumps, a total of 239 calls were received in the single month. Most of the victims were adults. The calls stepped up sharply toward the end of the month as gasoline supplies diminished with depletion of the state's monthly allocation, Dr. Schwartz says.

Most of the callers said they had swallowed one mouthful of gasoline.

Apparently none of the victims suffered prolonged health consequences from swallowing the motor fuel, although many suffered vomiting, coughing, choking and other symptoms.

If siphoning is necessary, a small pump-like siphoning device should be used, rather than sucking with the mouth to start the flow, she declares.

Whether the individuals were stealing gasoline or merely transferring some to another of their own autos was not known.

is so, says Charles H. Hennekens, MD, of Harvard's Channing Laboratory. It may be related to increases in high-density lipoproteins or decreases in low-density lipoproteins. These are body substances that are related to heart disease. Or there may be a personality factor. The more relaxed individual is satisfied with two drinks a day, while the more tense person either drinks heavily, or abstains.

However, in an accompanying editorial, W. P. Castilli, MD, of the National Heart Institute, Framingham, Mass., sounds a note of caution.

"With 17 million alcoholics in this country, perhaps we have a message for which this country is not yet ready," Dr. Castilli comments.

Zero intake of alcohol seems less healthful than a moderate intake, but higher intakes of alcohol are associated with increased rates of all of the well-known problems that alcohol produces, from nutritional, intestinal, nervous system, heart, blood, respiratory and cancer problems, he points out.

"The problem with all of this is that it may be dangerous to tell some people to take two drinks a day when, given their constitutional makeup, one could fairly predict they could not stop at two."

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# **MODERATE DRINKING MAY PREVENT HEART ATTACK, RESEARCHERS SAY**

Chicago — Moderate daily consumption of beverage alcohol may actually reduce the risk of fatal heart attack, says a report in the Nov. 2 Journal of the American Medical Association.

A Harvard Medical School research group studied a series of 568 married men who died of heart disease, and an equal number of matched controls. It was found that moderate drinkers — two beers, two glasses of wine, two highballs per day — were less likely to die a coronary death than total abstainers.

The researchers studied a number of other factors, such as cigarette smoking, previous heart disease and overweight. They determined that "the protective effect in coronary disease is actually due to alcohol itself rather than to other substances found in each type of drink."

There is only speculation thus far as to why this

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# **JOGGING IS GOOD FOR YOU, BUT IT ALSO MAY KILL YOU**

Chicago — Jogging is good for most of us, but for some it can be fatal, says a report in the Sept. 21 Journal of the American Medical Association.

In evaluating reports of 18 individuals who dropped dead during or shortly after jogging, researchers also found that there is no sure way your doctor can tell in advance whether vigorous exercise increases risk of heart attack for you.

Deaths during exercise are rare, but they do happen, says Paul D. Thompson, MD, of Brown University School of Medicine, Providence, R. I. In studies conducted while Dr. Thompson was still with the Stanford Heart Disease Prevention Program in California, researchers also learned that superior physical fitness



does not guarantee protection against exercise deaths.

Among the 18, doctors found that 13 men died of heart attack, while four men and a woman died of other causes, including one from heart stroke.

Premonitory symptoms of heart problems were noted in six of the 13 heart attack cases. There was no advance warning among the others.

All but four of the 18 had been exercising regularly for at least a year, and nine had exercised for three or more years. Of those who succumbed to heart attacks, one had exercised less than a month, and another was only nine days into walk-jogging program.

"We are convinced of the health benefits of regular physical exercise, but are concerned about the extravagant claims made by exercise enthusiasts," Dr. Thompson declares.

"With the explosive growth of jogging as a sport, there is an urgent need for definitive data on the risk-versus-benefit ratio of endurance exercise. Although the prevention of most exercise deaths depends on preventing coronary heart disease, and regular exercise may contribute to this goal, further studies are needed to identify those individuals who will profit from exercise training without excessive risk."

-----

#### HOSPITAL PATIENTS FOUND SAFE FROM AD-

#### DED "SUPERINFECTION"

Chicago — Much has been written concerning problems of patients in hospitals acquiring additional "superinfection" from the treatment itself. But in a major treatment area this just isn't true, says a report in the Sept. 21 Journal of the American Medical Association.

Among more than 14,000 hospitalized general medical patients in 22 Boston area hospitals who were receiving antibiotics, drug-related infection appears to have been an infrequent and most often minor problem, says Alexander M. Walker, MD, of the Boston Collaborative Drug Surveillance Program.

In a series of 14,077 hospitalized medical patients receiving antibiotics, superinfection developed in only 95, or 0.7 per cent, while receiving drug therapy, says Dr. Walker. Serious infections occurred with a frequency of less than one per 1,000 patients.

Patients 60 years or older had a risk of superinfection slightly higher than that of younger patients. Women were at slightly higher risk than men.

Writes Dr. Walker:

"While the risk of drug-related superinfection can never be dismissed, it was not an important hazard of antibiotic therapy in these patients."

The Boston Collaborative Drug Surveillance Program is a long-term study of useful drugs used in hospitals and all possible side effects, both good and bad. Hershel Jick, MD, and Jane Porter worked with Dr. Walker on this study.

#### A N U N C I O

Se alquila casa de dos pisos para oficina(s) frente al Hospital San Pablo, Bayamón, con derecho a subarrendamiento.

Para información: Lcdo. L. Ortiz, Teléfonos 785-0557 (oficina) y 785-3615 (residencia) noche.

## Tenuate<sup>®</sup> <sup>IV</sup>

(diethylpropion hydrochloride NF)

## Tenuate Dospan<sup>®</sup>

(diethylpropion hydrochloride NF) controlled-release

AVAILABLE ONLY ON PRESCRIPTION

### Brief Summary

**INDICATION:** Tenuate and Tenuate Dospan are indicated in the management of exogenous obesity as a short-term adjunct (a few weeks) in a regimen of weight reduction based on caloric restriction. The limited usefulness of agents of this class should be measured against possible risk factors inherent in their use such as those described below.

**CONTRAINDICATIONS:** Advanced arteriosclerosis, hyperthyroidism, known hypersensitivity, or idiosyncrasy to the sympathomimetic amines, glaucoma. Agitated states. Patients with a history of drug abuse. During or within 14 days following the administration of monoamine oxidase inhibitors, (hypertensive crises may result).

**WARNINGS:** If tolerance develops, the recommended dose should not be exceeded in an attempt to increase the effect; rather, the drug should be discontinued. Tenuate may impair the ability of the patient to engage in potentially hazardous activities such as operating machinery or driving a motor vehicle; the patient should therefore be cautioned accordingly. *Drug Dependence:* Tenuate has some chemical and pharmacologic similarities to the amphetamines and other related stimulant drugs that have been extensively abused. There have been reports of subjects becoming psychologically dependent on diethylpropion. The possibility of abuse should be kept in mind when evaluating the desirability of including a drug as part of a weight reduction program. Abuse of amphetamines and related drugs may be associated with varying degrees of psychologic dependence and social dysfunction which, in the case of certain drugs, may be severe. There are reports of patients who have increased the dosage to many times that recommended. Abrupt cessation following prolonged high dosage administration results in extreme fatigue and mental depression; changes are also noted on the sleep EEG. Manifestations of chronic intoxication with anorectic drugs include severe dermatoses, marked insomnia, irritability, hyperactivity, and personality changes. The most severe manifestation of chronic intoxications is psychosis, often clinically indistinguishable from schizophrenia. *Use in Pregnancy:* Although rat and human reproductive studies have not indicated adverse effects, the use of Tenuate by women who are pregnant or may become pregnant requires that the potential benefits be weighed against the potential risks. *Use in Children:* Tenuate is not recommended for use in children under 12 years of age.

**PRECAUTIONS:** Caution is to be exercised in prescribing Tenuate for patients with hypertension or with symptomatic cardiovascular disease, including arrhythmias. Tenuate should not be administered to patients with severe hypertension. Insulin requirements in diabetes mellitus may be altered in association with the use of Tenuate and the concomitant dietary regimen. Tenuate may decrease the hypotensive effect of guanethidine. The least amount feasible should be prescribed or dispensed at one time in order to minimize the possibility of overdosage. Reports suggest that Tenuate may increase convulsions in some epileptics. Therefore, epileptics receiving Tenuate should be carefully monitored. Titration of dose or discontinuance of Tenuate may be necessary.

**ADVERSE REACTIONS:** *Cardiovascular:* Palpitation, tachycardia, elevation of blood pressure, precordial pain, arrhythmia. One published report described T-wave changes in the ECG of a healthy young male after ingestion of diethylpropion hydrochloride. *Central Nervous System:* Overstimulation, nervousness, restlessness, dizziness, jitteriness, insomnia, anxiety, euphoria, depression, dysphoria, tremor, dyskinesia, mydriasis, drowsiness, malaise, headache, rarely psychotic episodes at recommended doses. In a few epileptics an increase in convulsive episodes has been reported. *Gastrointestinal:* Dryness of the mouth, unpleasant taste, nausea, vomiting, abdominal discomfort, diarrhea, constipation, other gastrointestinal disturbances. *Allergic:* Urticaria, rash, ecchymosis, erythema. *Endocrine:* impotence, changes in libido, gynecomastia, menstrual upset. *Hematopoietic System:* Bone marrow depression, agranulocytosis, leukopenia. *Miscellaneous:* A variety of miscellaneous adverse reactions has been reported by physicians. These include complaints such as dyspnea, hair loss, muscle pain, dysuria, increased sweating, and polyuria.

**DOSE AND ADMINISTRATION.** Tenuate (diethylpropion hydrochloride): One 25 mg. tablet three times daily, one hour before meals, and in mid-evening if desired to overcome night hunger. Tenuate Dospan (diethylpropion hydrochloride) controlled-release: One 75 mg. tablet daily, swallowed whole, in mid-morning. Tenuate is not recommended for use in children under 12 years of age.

**OVERDOSEAGE:** Manifestations of acute overdosage include restlessness, tremor, hyperreflexia, rapid respiration, confusion, assaultiveness, hallucinations, panic states. Fatigue and depression usually follow the central stimulation. Cardiovascular effects include arrhythmias, hypertension or hypotension and circulatory collapse. Gastrointestinal symptoms include nausea, vomiting, diarrhea, and abdominal cramps. Overdose of pharmacologically similar compounds has resulted in fatal poisoning, usually terminating in convulsions and coma. Management of acute Tenuate intoxication is largely symptomatic and includes lavage and sedation with a barbiturate. Experience with hemodialysis or peritoneal dialysis is inadequate to permit recommendation in this regard. Intravenous phenolamine (Regitine<sup>®</sup>) has been suggested on pharmacologic grounds for possible acute, severe hypertension, if this complicates Tenuate overdosage.

Product Information as of April, 1976

MERRELL-NATIONAL LABORATORIES Inc.  
Cayey, Puerto Rico 00633

Direct Medical Inquiries to

MERRELL-NATIONAL LABORATORIES  
Division of Richardson-Merrell Inc.  
Cincinnati, Ohio 45215, U.S.A.

Licensors of Merrell<sup>®</sup>

References: 1. Citations available on request from Medical Research Department, MERRELL-NATIONAL LABORATORIES, Cincinnati, Ohio 45215. 2. Hoekenga M.T. O'Dillon [Dillon], R.H. and Leyland, H.M. A comprehensive review of diethylpropion hydrochloride. In: Central Mechanisms of Anorectic Drugs, S. Garattini and R. Samanin, Ed., New York, Raven Press, 1978, pp. 391-404.

# Merrell

**Overweight may not always be simple...  
complications can develop.\***

**Complicated or not...**

# **Tenuate<sup>®</sup> Dospan<sup>®</sup> <sup>IV</sup>** **(diethylpropion hydrochloride NF)** **75 mg. controlled-release tablets**

## **A useful short-term adjunct in an indicated weight loss program.**

Overweight patients in certain diagnostic categories often require strict appetite control and a successful program of weight reduction may tend to diminish the incidence or severity of the complications in some patients. Diethylpropion hydrochloride has been reported useful in such patients and while it is not suggested that Tenuate itself in any way reduces the complications of overweight, it may have a useful place as a short-term adjunct in a prescribed dietary regimen. **Tenuate should not be administered to patients with severe hypertension; see additional Warnings and Precautions on the opposite page.**

## **In uncomplicated overweight.**

Many patients, on the other hand, present with excess fat but no disease. While this condition is often termed uncomplicated obesity, complications of both a social and a psychologic nature may be distressingly real for the patients. In these cases, a short-term regimen of Tenuate can help reinforce your dietary counsel during the important early weeks of an indicated weight loss program.

## **Clinical effectiveness.**

The anorectic effectiveness of diethylpropion hydrochloride is well documented. No less than 16 separate double-blind, placebo-controlled studies attest to its usefulness in daily practice.<sup>1</sup> And the unique chemistry of Tenuate provides "...anorectic potency with minimal overt central nervous system or cardiovascular stimulation."<sup>2</sup> Compared with the amphetamines, diethylpropion has minimal potential for abuse.

**Tenuate—it makes sense.  
And it's responsible medicine.**

\*Studies have shown that obesity is associated with an increased incidence of hypertension, symptomatic heart disease, adult-onset diabetes, and other diseases.

# **Merrell**



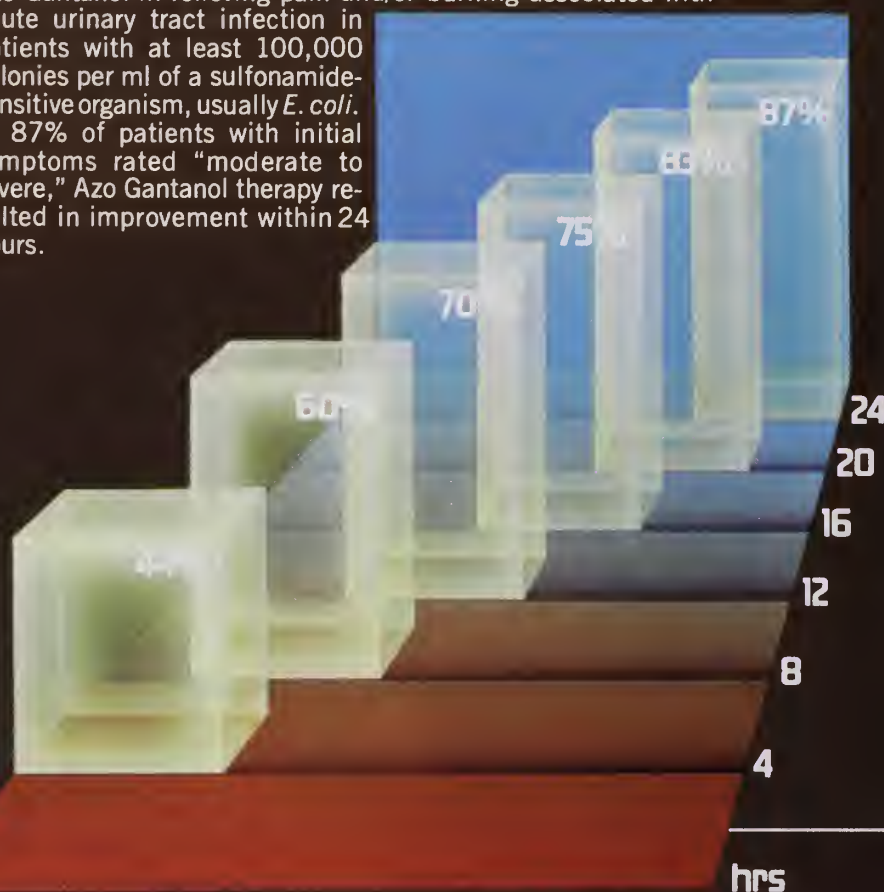
For prescribing information see opposite page



## Important data on the pain of acute cystitis:

# In 87% of patients studied (303 of 349), Azo Gantanol<sup>®</sup> reduced pain and/or burning within 24 hours\*

A controlled, multicenter study assessed the efficacy of Azo Gantanol in relieving pain and/or burning associated with acute urinary tract infection in patients with at least 100,000 colonies per ml of a sulfonamide-sensitive organism, usually *E. coli*. In 87% of patients with initial symptoms rated "moderate to severe," Azo Gantanol therapy resulted in improvement within 24 hours.



Before prescribing, please consult complete product information, a summary of which follows:

**Indications:** In adults, urinary tract infections complicated by pain (primarily pyelonephritis, pyelitis and cystitis) due to susceptible organisms (usually *E. coli*, *Klebsiella-Aerobacter*, *Staphylococcus aureus*, *Proteus mirabilis*, and, less frequently, *Proteus vulgaris*) in the absence of obstructive uropathy or foreign bodies. **Note:** Carefully coordinate *in vitro* sulfonamide sensitivity tests with bacteriologic and clinical response; add aminobenzoic acid to follow-up culture media. The increasing frequency of resistant organisms limits the usefulness of antibacterials including sulfonamides. Measure sulfonamide blood levels as variations may occur; 20 mg/100 ml should be maximum total level.

**Contraindications:** Children below age 12; sulfonamide hypersensitivity; pregnancy at term and during nursing period; because Azo Gantanol contains phenazopyridine hydrochloride it is contraindicated in glomerulonephritis, severe hepatitis, uremia, and pyelonephritis of pregnancy with G.I. disturbances.

**Warnings:** Safety during pregnancy not established. Deaths from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias have been reported and early clinical signs (sore throat, fever, pallor, purpura or jaundice) may indicate serious blood disorders. Frequent CBC and urinalysis with microscopic examination are recommended during sulfonamide therapy.

**Precautions:** Use cautiously in patients with impaired renal or hepatic function, severe allergy, bronchial asthma; in glucose-6-phosphate dehydrogenase-deficient individuals in whom dose-related hemolysis may occur. Maintain adequate fluid intake to prevent crystalluria and stone formation.

**Adverse Reactions:** **Blood dyscrasias** (agranulocytosis, aplastic anemia, thrombocytopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia); **allergic reactions** (erythema multiforme, skin eruptions, Stevens-Johnson syndrome, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis); **G.I. reactions** (nausea, emesis, abdominal pains, hepatitis, diarrhea, anorexia, pancreatitis and stomatitis); **CNS reactions** (headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo and insomnia); **miscellaneous reactions** (drug fever, chills, toxic nephrosis with oliguria and anuria, periarteritis nodosa and L. E. phenomenon). Due to certain chemical similarities with some goitrogens, diuretics (acetazolamide, thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia. Cross-sensitivity with these agents may exist.

**Dosage:** Azo Gantanol is intended for the acute, painful phase of urinary tract infections. **Usual adult dosage:** 2 Gm (4 tabs) initially, then 1 Gm (2 tabs) B.I.D. for up to 3 days. If pain persists, causes other than infection should be sought. After relief of pain has been obtained, continued treatment with Gantanol (sulfamethoxazole) may be considered.

**NOTE:** Patients should be told that the orange dye (phenazopyridine HCl) will color the urine.

**Supplied:** Tablets, red, film-coated, each containing 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl—bottles of 100 and 500

**ROCHE** Roche Laboratories  
Division of Hoffmann-La Roche  
Nutley, New Jersey 07110

Fast pain relief plus effective antibacterial action

# Azo Gantanol<sup>®</sup>

Each tablet contains 0.5 Gm sulfamethoxazole and 100 mg phenazopyridine HCl.

for  
the pain

for  
the pathogens



## A simple solution for beating the high cost of feeding babies.

Powdered Soyolac mixed with water (according to directions on the label) is an inexpensive, soy-based infant formula your patients can buy.

Up to 50% less expensive than ready-to-serve formulas.

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**Loma Linda**



# The heart of the matter in hypertension is the kidney

The kidney—not the heart—is the key to long-term arterial pressure control. Diuretics help the kidney excrete sodium, reduce fluid volume and lower blood pressure.

No diuretic blocks sodium retention longer than Hygroton.

In mild hypertension low-dose Hygroton 25 mg. An effective, conservative therapy.

## In mild hypertension

### Low-dose

# Hygroton<sup>®</sup> 25 mg. one a day

(chlorthalidone USP)

## Gets to the heart of the matter...simply

#### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema.

**Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

**Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. There is a possibility of exacerbation or activation of systemic lupus erythematosus with thiazides, which are related to chlorthalidone. This has not been reported with chlorthalidone. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

**Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous

patients in hot weather. Hyperuricemia may occur or gout be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum PBI levels without signs of thyroid disturbance.

**Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia, leukopenia, agranulocytosis, thrombocytopenia, aplastic anemia, purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hyperuricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate or severe, chlorthalidone dosage should be reduced or therapy withdrawn.

**Usual Dose:** One tablet daily.

**How Supplied:** Tablets—100 mg. (white, scored), 50 mg. (aqua) and 25 mg. (peach) in bottles of 100 and 1000; unit-dose blister packs, boxes of 100 (10 x 10 strips). Also, 100 mg. and 50 mg. in PAKs of 28 tablets, boxes of 5.

**USV**  
LABORATORIES

USV Laboratories Inc.  
Manati, P.R. 00701



**Before prescribing, please consult complete product information, a summary of which follows:**

The effectiveness of Valium (diazepam) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindications:** Tablets in children under 6 months of age, known hypersensitivity; acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy

**Warnings:** As with most CNS-acting drugs, caution against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Withdrawal symptoms (similar to those with barbiturates, alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal/muscle cramps, vomiting, sweating). Keep addiction-prone individuals (drug addicts or alcoholics) under careful surveillance because of predisposition to habituation/dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations, as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**ORAL:** Advise patients against simultaneous ingestion of alcohol and other CNS depressants.

Not of value in treatment of psychotic patients; should not be employed in lieu of appropriate treatment. When using oral form adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increase in dosage of standard anticonvulsant medication; abrupt withdrawal in such cases may be associated with temporary increase in frequency and/or severity of seizures.

**INJECTABLE:** To reduce the possibility of venous thrombosis, phlebitis, local irritation, swelling, and, rarely, vascular impairment when used I.V.: inject slowly, taking at least one minute for each 5 mg (1 ml) given; do not use small veins, i.e., dorsum of hand or wrist; use extreme care to avoid intra-arterial administration or extravasation. Do not mix or dilute Valium with other solutions or drugs in syringe or infusion flask. If it is not feasible to administer Valium directly I.V., it may be injected slowly through the infusion tubing as close as possible to the vein insertion.

Administer with extreme care to elderly, very ill, those with limited pulmonary reserve because of possibility of apnea and/or cardiac arrest; concomitant use of barbiturates, alcohol or other CNS depressants increases depression with increased risk of apnea; have resuscitative facilities available. When used with narcotic analgesic eliminate or reduce narcotic dosage at least 1/3, administer in small increments. Should not be administered to patients in shock, coma, acute alcoholic intoxication with depression of vital signs.

Has precipitated tonic status epilepticus in patients treated for petit mal status or petit mal variant status.

Withdrawal symptoms (similar to those with barbiturates, alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal/muscle cramps, vomiting, sweating). Keep addiction-prone individuals under careful surveillance because of predisposition to habituation/dependence. Not recommended for OB use.

Efficacy/safety not established in neonates (age 30 days or less); prolonged CNS depression observed. In children, give slowly (up to 0.25 mg/kg over 3 minutes) to avoid apnea or prolonged somnolence; can be repeated after 15 to 30 minutes. If no relief after third administration, appropriate adjunctive therapy is recommended.

**Precautions:** If combined with other psychotropics or anticonvulsants, carefully consider individual pharmacologic effects—particularly with known compounds which may potentiate action of Valium (diazepam), i.e., phenothiazines, narcotics, barbiturates, MAO inhibitors and antidepressants. Protective measures indicated in highly anxious patients with accompanying depression who may have suicidal tendencies. Observe usual precautions in impaired hepatic function; avoid accumulation in patients with compromised kidney function. Limit oral dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation (initially 2 to 2½ mg once or twice daily, increasing gradually as needed or tolerated).

**INJECTABLE:** Although promptly controlled, seizures may return, readminister if necessary, not recommended for long-term maintenance therapy. Laryngospasm/increased cough reflex are possible during peroral endoscopic procedures, use topical anesthetic have necessary countermeasures available. Hypotension or muscular weakness possible, particularly when used with narcotics, barbiturates or alcohol. Use lower doses (2 to 5 mg) for elderly/debilitated.

**Adverse Reactions:** Side effects most commonly reported were drowsiness, fatigue, ataxia. Infrequently encountered were confusion, constipation, depression, diplopia, dysarthria, headache, hypotension, incontinence, jaundice, changes in libido, nausea, changes in salivation, skin rash, slurred speech, tremor, urinary retention, vertigo, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances and stimulation have been reported, should these occur, discontinue drug. Because of isolated reports of neutropenia and jaundice, periodic blood counts, liver function tests advisable during long-term therapy. Minor changes in EEG patterns, usually low-voltage fast activity, have been observed in patients during and after Valium (diazepam) therapy and are of no known significance.

**INJECTABLE:** Venous thrombosis/phlebitis at injection site, hypoactivity, syncope, bradycardia, cardiovascular collapse, nystagmus, urticaria, hiccups, neutropenia.

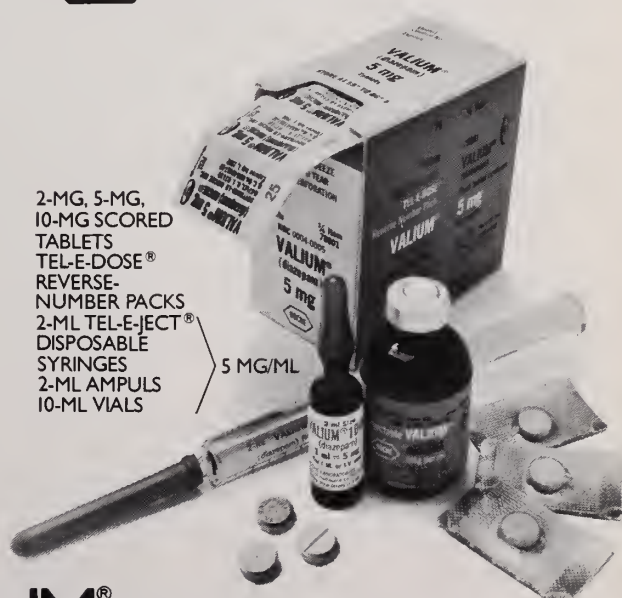
In peroral endoscopic procedures, coughing, depressed respiration, dyspnea, hyperventilation, laryngospasm/pain in throat or chest have been reported.

**Management of Overdosage:** Manifestations include somnolence, confusion, coma, diminished reflexes. Monitor respiration, pulse, blood pressure, employ general supportive measures, I.V. fluids, adequate airway. Use levarterenol or metaraminol for hypotension, caffeine and sodium benzoate for CNS-depressive effects. Dialysis is of limited value.

**Supplied:** Tablets, 2 mg, 5 mg and 10 mg, bottles of 100 and 500; Tel-E-Dose® (unit dose) packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10, Prescription Paks of 50, available singly and in trays of 10. Ampuls, 2 ml, boxes of 10, Vials, 10 ml, boxes of 1, Tel-E-Ject® (disposable syringes), 2 ml, boxes of 10. Each ml contains 5 mg diazepam, compounded with 40% propylene glycol, 10% ethyl alcohol, 5% sodium benzoate and benzoic acid as buffer, and 1.5% benzyl alcohol as preservative.



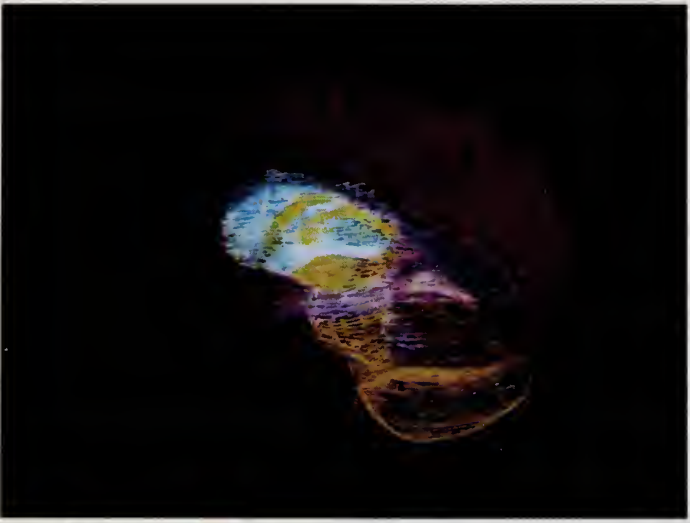
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**ONLY VALIUM® (diazepam)  
GIVES YOU THIS CHOICE OF DOSAGE  
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SKELETAL MUSCLE  
RELAXANT



ONLY **VALIUM**<sup>®</sup>  
(diazepam)<sup>IV</sup>  
HAS THESE TWO  
DISTINCT EFFECTS

Please see preceding page for a summary of product information.

ROCHE

DISPLAY  
SHELVES



# BOLETIN

## ASOCIACION MEDICA DE PUERTORICO

### C O N T E N I D O

SPINAL CORD COMPRESSION BY METASTASES:  
A NEUROSURGICAL AND ONCOLOGIST EMERGENCY

TUBERCULOSIS: CONCEPTOS ACTUALES - PARTE I

EFFECT OF ORAL CONTRACEPTIVE ON HEMATOCRIT LEVEL

CARDIAC PACEMAKER AND PREGNANCY -  
A FOLLOW UP AND ANNOTATION

EDITORIAL: LA IMPORTANCIA DE LOS SERVICIOS DE  
REHABILITACION EN UN HOSPITAL GENERAL

CARTA AL EDITOR

ABSTRACTOS DE LITERATURA MEDICA

NOTICIAS

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VOL. 71

NUM. 11

NOVIEMBRE 1979

THE FRANCIS A. COWNTWAY  
LIBRARY OF MEDICINE

THE FRANCIS A. COWNTWAY  
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BOSTON



# A character all its own.



Valium (diazepam/Roche)  
is a benzodiazepine with a  
character all its own.

Pharmacologically, it is a potent skeletal muscle relaxant and anticonvulsant (in adjunctive use), as well as an antianxiety agent. Pharmacokinetically, only Valium provides active *diazepam* as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

## Valium<sup>®</sup> <sup>IV</sup> diazepam/Roche

2-mg, 5-mg, 10-mg scored tablets  
a prudent choice in psychic  
tension and anxiety

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

**Dosage:** Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

**Supplied:** Valium<sup>®</sup> (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose<sup>®</sup> packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.



Roche Laboratories  
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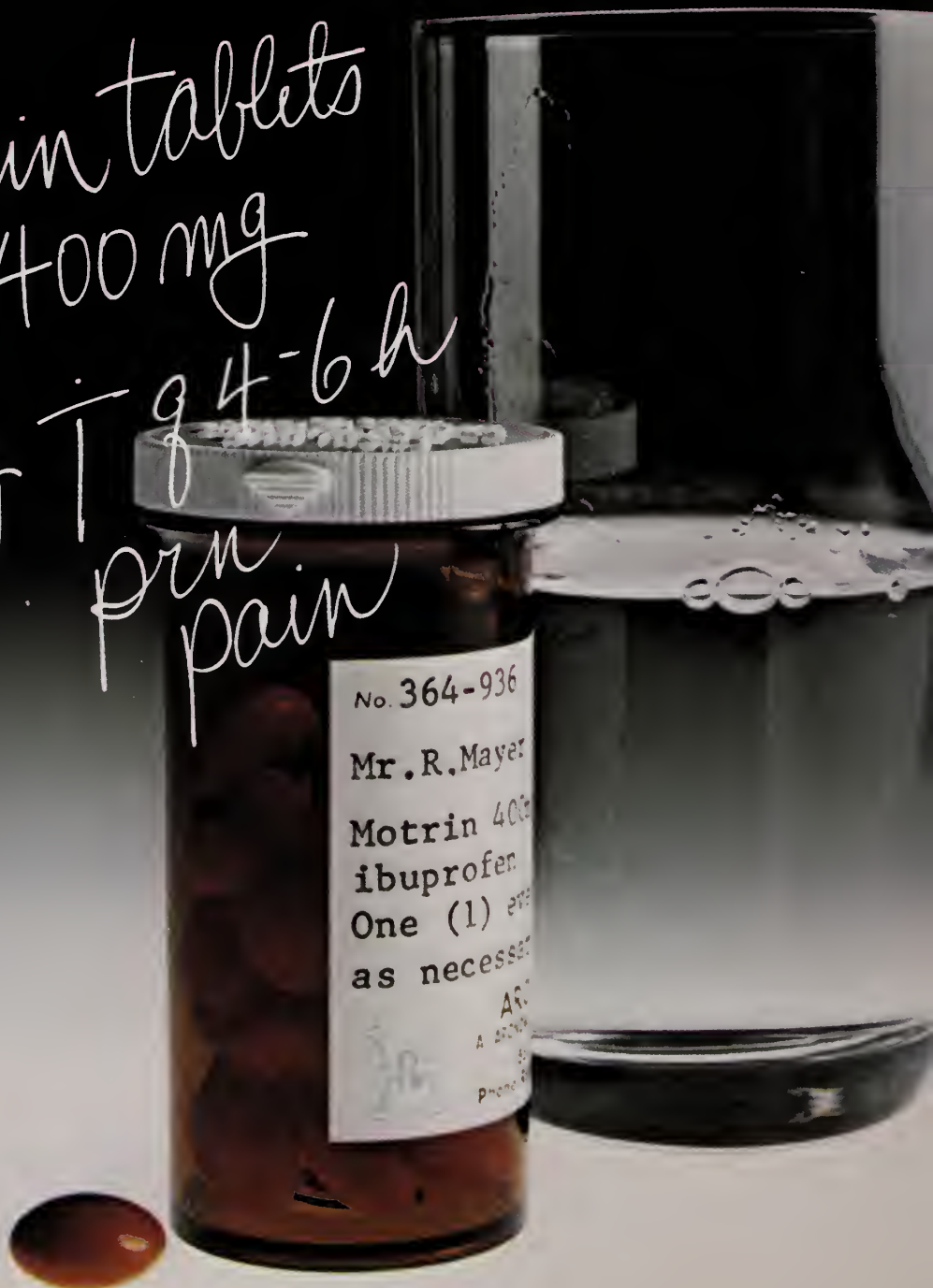
The Upjohn Company  
announces  
a new  
indication for  
Motrin<sup>®</sup>  
(ibuprofen)



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MAR 6 1980

A well-tolerated, nonnarcotic prescription for pain

Motrin tablets  
400 mg  
Sig T q 4-6 h  
prn  
pain





# Motrin now proved an effective analgesic for mild to moderate pain

Motrin 400 mg provided greater relief of pain than did propoxyphene 65 mg in controlled clinical pain studies.

Time after drug administration (hour)		.5	1	2	3	4
Mean relief-of-pain scores* (No. patients reporting)	Motrin 400 mg ibuprofen	.89 (108)	1.25 (108)	1.36 (108)	1.28 (107)	1.19 (106)
	Darvon 65 mg propoxyphene	.66 (100)	.99 (99)	1.13 (96)	.99 (96)	.80 (96)
Statistical significance		p<0.02	p<0.01	p<0.05	p<0.02	p<0.002

\*0 = No relief    1 = Partial relief    2 = Complete relief

Data on file at The Upjohn Company

Motrin demonstrated statistically significant greater relief of pain than did Darvon at all time intervals.

**Motrin** 400<sup>TABLETS</sup>mg  
ibuprofen, Upjohn

- Not a narcotic • Not addictive • Not habit forming
- Rapid analgesic action • Indicated in acute and chronic pain
- Well tolerated. The most common side effect with Motrin is mild gastrointestinal disturbance.

Please turn the page for a brief summary of prescribing information.

**Motrin<sup>®</sup>** (ibuprofen)

now proved an  
effective analgesic for  
mild to moderate pain

**Motrin<sup>®</sup> Tablets** (ibuprofen, Upjohn)

**Indications and Usage:** Treatment of signs and symptoms of rheumatoid arthritis and osteoarthritis during acute flares and in long-term management. Safety and efficacy have not been established in Functional Class IV rheumatoid arthritis.

Relief of mild to moderate pain.

**Contraindications:** Individuals hypersensitive to it, or with the syndrome of nasal polyps, angioedema and bronchospastic reactivity to aspirin or other nonsteroidal anti-inflammatory agents (see WARNINGS).

**Warnings:** Anaphylactoid reactions have occurred in patients with aspirin hypersensitivity (see CONTRAINDICATIONS).

Peptic ulceration and gastrointestinal bleeding, sometimes severe, have been reported. Ulceration, perforation, and bleeding may end fatally. An association has not been established. Motrin should be given under close supervision to patients with a history of upper gastrointestinal tract disease, only after consulting ADVERSE REACTIONS.

In patients with active peptic ulcer and active rheumatoid arthritis, nonulcerogenic drugs, such as gold, should be tried. If Motrin must be given, the patient should be under close supervision for signs of ulcer perforation or gastrointestinal bleeding.

**Precautions:** Blurred and/or diminished vision, scotomata, and/or changes in color vision have been reported. If these develop, discontinue Motrin and the patient should have an ophthalmologic examination, including central visual fields.

Fluid retention and edema have been associated with Motrin; use with caution in patients with a history of cardiac decompensation.

Motrin can inhibit platelet aggregation and prolong bleeding time. Use with caution in persons with intrinsic coagulation defects and those on anticoagulant therapy.

Patients should report signs or symptoms of gastrointestinal ulceration or bleeding, blurred vision or other eye symptoms, skin rash, weight gain, or edema.

To avoid exacerbation of disease or adrenal insufficiency, patients on prolonged corticosteroid therapy should have therapy tapered slowly when Motrin is added.

**Drug interactions.** Aspirin: used concomitantly may decrease Motrin blood levels. Coumarin: Bleeding has been reported in patients taking Motrin and coumarin.

**Pregnancy and nursing mothers:** Motrin should not be taken during pregnancy or by nursing mothers.

#### Adverse Reactions

*Incidence greater than 1%*

**Gastrointestinal:** The most frequent type of adverse reaction occurring with Motrin is gastrointestinal (4% to 16%). This includes nausea,\* epigastric pain,\* heartburn,\* diarrhea, abdominal distress, nausea and vomiting, indigestion, constipation, abdominal cramps or pain, fullness of the GI tract (bloating and flatulence). **Central Nervous System:** Dizziness,\* headache, nervousness. **Dermatologic:** Rash\* (including maculopapular type), pruritus. **Special Senses:** Tinnitus. **Metabolic:** Decreased appetite, edema, fluid retention. Fluid retention generally responds promptly to drug discontinuation (see PRECAUTIONS).

\*Incidence 3% to 9%.

*Incidence less than 1 in 100*

**Gastrointestinal:** Upper GI ulcer with bleeding and/or perforation, hemorrhage, melena. **Central Nervous System:** Depression, insomnia. **Dermatologic:** Vesiculobullous eruptions, urticaria, erythema multiforme. **Cardiovascular:** Congestive heart failure in patients with marginal cardiac function, elevated blood pressure. **Special Senses:** Amblyopia (see PRECAUTIONS). **Hematologic:** Leukopenia, decreased hemoglobin and hematocrit.

*Causal relationship unknown*

**Gastrointestinal:** Hepatitis, jaundice, abnormal liver function. **Central Nervous System:** Paresthesias, hallucinations, dream abnormalities. **Dermatologic:** Alopecia, Stevens-Johnson syndrome. **Special Senses:** Conjunctivitis, diplopia, optic neuritis. **Hematologic:** Hemolytic anemia, thrombocytopenia, granulocytopenia, bleeding episodes. **Allergic:** Fever, serum sickness, lupus erythematosus syndrome. **Endocrine:** Gynecomastia, hypoglycemia. **Cardiovascular:** Arrhythmias. **Renal:** Decreased creatinine clearance, polyuria, azotemia.

**Overdosage:** In cases of acute overdosage, the stomach should be emptied. The drug is acidic and excreted in the urine, so alkaline diuresis may be beneficial.

**Dosage and Administration:** Rheumatoid and osteoarthritis, including flares of chronic disease: Suggested dosage is 300, 400 or 600 mg t.i.d. or q.i.d. Mild to moderate pain: 400 mg every 4 to 6 hours as necessary for relief of pain.

Do not exceed 2400 mg per day.

**Caution:** Federal law prohibits dispensing without prescription.

For additional product information, see your Upjohn representative or consult the package insert.

MED B-4-S

**Upjohn** THE UPJOHN COMPANY  
Kalamazoo, Michigan 49001 USA

**ALDORIL<sup>®</sup>**  
containing methyldopa and hydrochlorothiazide

**TABLETS**

#### **ALDORIL<sup>®</sup>-25**

containing 250 mg ALDOMET<sup>®</sup> (Methyldopa, MSD)  
and 25 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

**TABLETS**

#### **ALDORIL<sup>®</sup>-15**

containing 250 mg ALDOMET<sup>®</sup> (Methyldopa, MSD)  
and 15 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

**TABLETS**

#### **ALDORIL<sup>®</sup> D30**

containing 500 mg ALDOMET<sup>®</sup> (Methyldopa, MSD)  
and 30 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

**TABLETS**

#### **ALDORIL<sup>®</sup> D50**

containing 500 mg ALDOMET<sup>®</sup> (Methyldopa, MSD)  
and 50 mg HydroDIURIL<sup>®</sup> (Hydrochlorothiazide, MSD)

Merck Sharp & Dohme, Division of  
Merck & Co., Inc., West Point, PA 19486

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ASOCIACION MEDICA DE PUERTO RICO

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Fundado en 1903

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* Spinal Cord Compression by Metastases - A Neurosurgical and Oncological Emergency	411
<i>Arturo A. Ydrach, MD, Víctor A. Marcial, MD and Hiram Mercado, MD</i>	
<p>Ydrach y sus colaboradores presentan y discuten 2 pacientes con compresión del cordón espinal por lesiones metastáticas. De acuerdo a los autores esta es una de las emergencias onco-neuroquirúrgicas más frecuente con que se puede encontrar aquellos médicos envueltos en el manejo clínico de pacientes con cáncer. Los autores hacen un resumen excelente del diagnóstico y tratamiento de esta condición. Concluyen que el paciente oncológico merece medidas preventivas para evitar de esta forma los resultados causados por compresión del cordón espinal.</p>	
* Tuberculosis: Conceptos Actuales - Parte I	417
<i>Ramón Ramírez Ronda, MD y Carlos H. Ramírez Ronda, MD, FACP</i>	
<p>En este artículo Ramírez Ronda presenta la magnitud y espectro del problema de tuberculosis en Puerto Rico. Describen los autores la patogénesis y manifestaciones clínicas de la tuberculosis primaria y la tuberculosis pulmonar crónica. Aunque la relación entre el desarrollo de hipersensitividad tardía después de una infección primaria y la inmunidad celular sigue siendo controversial, los autores presentan en forma concisa los eventos inmunológicos que ocurren después de una estimulación antigénica primaria. La presentación de la quimioterapia de tuberculosis pulmonar será de gran interés para todos los lectores del Boletín.</p>	
* Effect of Oral Contraceptive on Hematocrit Level	425
<i>Abelardo Fuertes-De la Haba, MD, DPH, FACOG, Héctor E. Ortiz Pérez, MD Ishver S. Bangdiwala, PhD, FASA and Carlos A. Roure, MD</i>	
<p>In this article Fuertes de la Haba y sus colaboradores presentan los resultados de un estudio diseñado para evaluar los efectos de contraceptivos orales en el hematocrito de 4,798 mujeres admitidas al Proyecto Materno-Infantil en la Escuela de Medicina de la Universidad de Puerto Rico. Este grupo se comparó con 4,886 mujeres con contraceptivos vaginales. El análisis estadístico no demostró diferencias significativas entre los valores medios de hematocrito. Aunque se ha reportado alteraciones en el metabolismo de ciertas vitaminas y minerales relacionado al uso de contraceptivos orales, estos no afectan el nivel de hemoglobina sanguínea irrespectivamente del tiempo que han sido usados.</p>	
* Cardiac Pacemakers and Pregnancy - A Follow Up and Annotation	434
<i>Charles D. Johnson, MD</i>	
<p>En 1977 Dr. Johnson reportó en este Boletín una paciente de 16 años a quien se le implantó un marcapaso temporero debido a bloqueo atrio-ventricular completo. Subsiguientemente la paciente quedó embarazada. Después de un embarazo de 9 meses tuvo un parto vaginal sin complicaciones. En este artículo, el autor presenta el seguimiento clínico de esta paciente en los últimos dos años. De igual forma resume la literatura sobre el uso de marcapasos durante el embarazo y los cambios fisiológicos que los acompañan.</p>	
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# Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

## Christmas Safety Pointers Are Listed

### Safe Yule Possible

Glass Christmas tree ornaments definitely are *not* recommended for baby's diet this holiday season.

Absurd statement? Of course. But not as absurd as you might think. A good many small tots will pop a shiny glass bulb or ornament into their mouths this Christmas season, as always.

Christmas is a time of bright little lights on a tree in the parlor, of shiny glass ornaments and decorations, of spun glass filaments, of toys that sometimes have sharp, rough edges, of lots of candy, nuts and other rich edibles.

These all are a part of Christmas, and no one is suggesting there's anything wrong about it. But the American Medical Association once again points out that there are safety hazards at the Christmas season that aren't usually encountered the rest of the year.

Check your old strings of tree lights and discard those that are worn or brittle. If

there are very small children around discard burnt bulbs with caution, making certain baby can't retrieve them from a waste basket.

Keep glass ornaments and filmy glass "angel hair" out of baby's reach. The ornaments crumble readily into sharp slivers.

Select toys with a minimum of sharp, rough edges, toys that won't burn quickly if flicked through a candle flame, toys that are large enough so that baby can't swallow them.

Electrical toys should be selected with safety in mind. Is the wiring intact and strong, or is it loose and flimsy?

Air rifles, sling shots, archery sets and other missile throwing toys are obviously dangerous if carelessly used. Set up target ranges and make certain the youngster is taught to use the toy properly and safely.

The list could be continued, but you can make your own. The prime objective of an article such as this one is to remind parents that in the bustle and excitement of Christmas accidents can happen. Certainly no one wants to spoil a holiday with undue worry about safety. Make your plans for a safe Christmas, then enjoy it to the hilt.



December, 1979  
Frank Chappell  
Science New Editor:  
AMA

**In pediatric infections**

6

# Septra<sup>®</sup>

Each teaspoonful (5 ml) contains:  
40 mg trimethoprim and 200 mg sulfamethoxazole

## Suspension B.I.D.

**Acute  
Otitis  
Media**



## where the action is.



# In acute otitis media

Septra Suspension provides effective antibacterial action against susceptible strains of H influenzae and S pneumoniae (D pneumoniae), the pathogens most likely to cause acute otitis media in children.

Septra Suspension is useful in many patients, but especially in those with penicillin allergy or with infections caused by ampicillin-resistant H influenzae. Limited clinical data are presently available on the effectiveness of treatment of acute otitis media with Septra when the infection is due to H influenzae resistant to ampicillin. However, in vitro data is highly favorable; when over 200 strains of ampicillin-resistant H influenzae were tested, all proved susceptible to TMP/SMX.\*

And unlike most other antibacterials for the treatment of acute otitis media, Septra Suspension is administered on a convenient b.i.d. dosage schedule. The cherry-flavored suspension is well accepted by children.



# In recurrent urinary tract infections

Septra Suspension provides effective antibacterial action in urine and blood against susceptible strains of E coli, Klebsiella-Enterobacter and Proteus. Whether the infection centers in the kidneys or bladder, Septra Suspension maintains effective levels at the site of the infection with just two doses a day.

Adequate fluid intake should be maintained and frequent urinalyses with careful microscopic examination performed during Septra therapy. Septra is contraindicated in infants under two months of age.

\*In vitro data do not necessarily correlate with clinical results. Data on file, Burroughs Wellcome Co.

NOTE: Septra should not be used in the treatment of streptococcal pharyngitis.

*Please see prescribing information on next page.*



Wellcome

**Burroughs Wellcome Co.**  
Research Triangle Park  
North Carolina 27709

# Septra® Suspension B.I.D.

Each teaspoonful (5 ml) contains: 40 mg trimethoprim and 200 mg sulfamethoxazole

# Septra® DS B.I.D.

Each tablet contains: 160 mg trimethoprim and 800 mg sulfamethoxazole

Septra® DS Tablets Double Strength  
Septra® Tablets  
Septra® Suspension

**INDICATIONS AND USAGE:**

**URINARY TRACT INFECTIONS:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morganii*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

**NOTE:** Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

**ACUTE OTITIS MEDIA:** For the treatment of acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to *Haemophilus influenzae* resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.

**SHIGELLOSIS:** For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

**PNEUMOCYSTIS CARINII PNEUMONITIS:** For the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

**CONTRAINDICATIONS:** Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

**WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.**

Clinical studies have documented that patients with Group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

**PRECAUTIONS:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

**ADVERSE REACTIONS:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. *Blood Dyscrasias:* Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. *Allergic Reactions:* Erythema multiforme, Stevens-Johnson

syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. *Gastrointestinal Reactions:* Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. *C.N.S. Reactions:* Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. *Miscellaneous Reactions:* Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L. E. phenomenon have occurred.

Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

**DOSAGE AND ADMINISTRATION:** Not recommended for use in infants less than two months of age.

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:**

**Adults:** The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

**Children:** The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose—every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 ( 5 ml)	½
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1½
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

**PNEUMOCYSTIS CARINII PNEUMONITIS:**

The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose—every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 ( 5 ml)	½
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1½
70	32	4 (20 ml)	2 (or 1 DS tablet)

**HOW SUPPLIED:** TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

**ORAL SUSPENSION,** containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.



Burroughs Wellcome Co.  
Research Triangle Park  
North Carolina 27709

# SPINAL CORD COMPRESSION BY METASTASES- A NEUROSURGICAL AND ONCOLOGICAL EMERGENCY

Arturo A. Ydrach, MD, Víctor A. Marcial, MD and Hiram Mercado, MD

**Summary:** The case report of two young patients with spinal cord compression by metastatic disease are presented. The diagnosis and management of this serious, and frequently not diagnosed, oncologic emergency is also presented. The two cases had complete preservation of neurologic function. One case was treated by radiotherapy alone, and the other by laminectomy and radiotherapy.

**Resumen:** Los casos de dos pacientes con compresión por metástasis del cordón espinal son presentados. El diagnóstico y tratamiento de esta emergencia oncológica es presentado. La radioterapia solamente acompañada de esteroides se utilizó en el tratamiento de un caso; y la laminectomía con decompresión y radioterapia en el otro caso. Ambos casos tuvieron excelentes resultados con la preservación de función neurológica.

## Introduction

The presence of metastatic cells in the epidural space can produce spinal cord com-

pression which can progress to complete paraplegia. Metastatic epidural metastases are frequent in patients with disseminated malignant disease of many sites, and constitute a serious neurosurgical and oncological emergency. The diagnosis and management must be expedited to prevent irreversible ischemic damage to the spinal cord with its accompanying physical and psychological consequences to patient and family.

This paper will present two cases of young patients recently seen by us at the Metropolitan Hospital where excellent preservation of neurologic function was obtained with radiotherapy alone in one case, and with surgical laminectomy and radiotherapy in the other. Also, the diagnosis and management of this oncologic emergency based on pertinent medical literature review, will be discussed.

## Case Reports

*Case No. 1:* A 17-year-old male diagnosed on 3/3/78 by open thoracotomy to have "thymoma". He received post-operative radiotherapy to mediastinum up to 5,000r (3/15/78 to 5/10/78). Early in July 1978 he developed low back pain below waist, radiating to both knees. Pain was severe and increased with flexion of head. He had no external evidence of disease on exam. He had negative chest film, negative bone scan and negative bone survey. He was admitted for complete work-up on 7/28/78 at Metropolitan Hospital due to severe pain in the back

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and unable to sleep for two days prior to admission. On 7/29/70 neurologist evaluation showed: alert, oriented. Cranial nerves - negative, discs and pupils normal. Strength symmetrical: DTR's - biceps and triceps normal. Sensation and coordination within normal limits. Knee jerk one plus bilaterally. Ankle jerks three plus bilaterally. Plantar-flexor - sensation symmetrical. Straight leg raising does not aggravate back pain. Left flank, L1 dermatome there is a strip of Hypoesthesia anterolaterally. Lumbar puncture - 240mm. C.S.F. opening pressure, and Protein - 150 mg. percent. On 7/30/78 high dose of Dexamethasone was started due to severe pain despite strong analgesics. 100 mgs. Dexamethasone I. V. push, and 24 mgs. Dexamethasone I. V. Q.I.D. by 3 days and taper.

The patient had a dramatic response to high dose of Dexamethasone with complete pain resolution in 24 hours. On August 1, 1978 myelogram showed total block to cephalad flow of oil at T12-L1 secondary to extradural mass.

Radiotherapy began 3,000r (August 2, 30/78) 150r/day and was discharged on August 8/78 ambulating and free of pain. Chemotherapy started after radiotherapy was given to spine - (Oncovin, CTX and Prednisone). He had three admissions from September/78 to February /79, but did not develop paraplegia until April/79.

On April/79 he developed paraplegia in Florida while receiving Laetrile. He was transferred to Puerto Rico on 4/28/79 and his disease progressed to death on 5/12/79, about 14 months after finding a mediastinal mass on X-ray and about 8 months after radiation treatment to first extradural metastasis.

#### *Comments:*

The case shows that one can have total block on myelography with few objective neurologic findings. The dramatic response of pain to high dose Dexamethasone is instructive. The response was maintained for eight months post radiotherapy when paraplegia occurred.

*Case No. 2:* A 29-year-old female admitted on 5/21/79 to Metropolitan Hospital with lytic lesion

T-10 and back pain of a few month's duration. H. P. I. - December 9/77 - at age 27 she had a left modified radical mastectomy and the pathology showed medullary carcinoma with negative lymph nodes. She did well for the following year. In January/79 she developed back pain and a chest film two months prior to admission showed metastatic nodules to right lower lobe and left upper lobe. On April 30, 1979 bilateral oophorectomy was done elsewhere due to bilateral pulmonary metastatic disease.

On May 21/79 X-ray was done for back pain which showed lytic lesion T-10. Nevertheless, bone scans done on January and May/79 were negative. She was started on radiotherapy to T-10 on May 21/79 at 300 rads daily to 1,500 rads (5 days). On May 22/79 neurosurgery evaluation only found numbness on thighs. DTR's three plus, plantar-flexor, sensory intact, motor - no weakness. On May 24/79 myelogram showed complete block to cephalad flow of dye at T-9 T-10, with appearance of extradural mass lesion. On May 27/79 decompression laminectomy was done and tumor was found to extend from T-9 to T-11. Pathology showed metastatic carcinoma of breast. Radiotherapy was restarted one week post-operatively at 300 rads daily to 4,500 rads to area of lesion. On June 13/79 she was discharged to end radiotherapy as out-patient, using Taylor Knight Brace. She was sent home on Tamoxiphen 10 mgs. P. O. B. I. D. The lung lesions are to be followed for decision on future chemotherapy.

#### *Comments:*

The case again shows that one can have a total block on myelography with no objective neurologic findings. Radiotherapy alone did not improve the back pain after 1,500 r in 5 days. Decompression laminectomy produced immediate relief of pain. The patient is ambulatory and receiving chemotherapy.

### **Discussion**

#### *Presenting Symptoms:*

Early diagnosis of spinal cord compression can often be difficult due to the lack of neuro-

logic signs. Almost every case has central back pain with or without radicular pain. Pain is followed at variable intervals by other symptoms. Motor dysfunction often precedes paresthesias, but the two may develop concomitantly. In experiments with dogs where mechanical extradural pressure was used to achieve spinal cord compression, Tarlov showed that neurological deficits progressed from initial motor loss to subsequent sensory loss (1).

Patients commonly describe numbness and tingling of lower extremities as our case No. 2, and sensory changes are almost always present before the patient develops paraplegia. Metastases to conus medullaris and cauda equina produce saddle anesthesia, with loss of urethral, vaginal and rectal sensation and impaired control of micturition. Loss of sphincter control is a late manifestation of cord compression, but disturbances of micturition may occur early.

### Diagnosis

Once the diagnosis of cord compression is suspected it must be confirmed. The compression can be due to metastases in the vertebrae with and without collapse, and, less commonly, to metastases growing directly in the epidural space.

The distribution of metastases is similar in several series: cervical, 10 percent, thoracic, 70 percent, lumbosacral, 20 percent (2).

Radiographs of the spine are positive in 70-80 percent of patients. The abnormalities include erosion and loss of pedicles, partial or complete collapse of vertebral bodies, and paraspinal soft tissue masses.

Complete investigation should include: 1) Plain X-rays of spine, 2) Bone scan, 3) Complete neurologic evaluation including lumbar puncture (most cases have protein level more

than 100mg percent and, 4) Lumbar myelogram. To establish the exact location and extent of any spinal cord compression, myelography is essential for both the neurosurgeon and the radiotherapist. The typical myelographic finding is an extradural mass causing complete obstruction, as in cases No. 1 and No. 2. The differential diagnosis is usually not difficult, especially in the presence of bony involvement, but should include: 1) 1<sup>o</sup> Benign tumors (i.e. neurofibroma and disc), 2) Radiation myelopathy, 3) Epidural hematomas, 4) Myelopathy due to non-metastatic lesions (i.e., subacute necrotic myelopathy). Most diseases that can mimic cord compression by tumor can usually be differentiated by myelography except epidural hemorrhage, which can be seen in patients with thrombocytopenia. At times a suspected herniated disc may be found at laminectomy to be a tumor.

If there is a complete block, the upper limits can be delineated by introduction of contrast thru cisternal puncture. It is important to examine the entire cord at myelography, since metastases to epidural space are frequently multiple.

Cerebrospinal fluid should be withdrawn at time of myelography and sent for: cells, protein and sugar. Metastases from carcinoma of the lung, breast carcinoma, lymphoma, and an unknown primary tumor, are the most common causes and are responsible for 50 percent of cord compressions (2).

Complete epidural block is often present with minimal or no neurologic signs, as depicted in our two-case reports. The reluctance to proceed with myelography in the absence of neurologic signs may result in progression to complete paraplegia.

Cord compression from lymphomas are presumed to occur as a result of growth of tumors from involved retro-peritoneal and mediastinal lymph nodes thru intervertebral foramina.

Epidural spinal lesions are an autopsy finding in 5 percent of patients with cancer (3). In view of the frequency of this complication in patients with malignant disease, all physicians should have a high index of suspicion in patients with cancer who show persistent back pain. The frequent use of myelography to exclude spinal cord compression is justified to detect early cord compression. Some authors have said that perhaps all patients with a known malignancy and persistent back pain should have a myelogram (4).

### Treatment

The appropriate treatment for spinal cord compression due to metastatic disease depends on the type of tumor, the rapidity of onset of symptoms, and the degree and duration of the block. The controversy lies in which patients to use radiotherapy alone combined with high dose of steroids, versus surgical decompression laminectomy followed by post-operative radiotherapy. The authors know of no good randomized controlled clinical trial comparing results of the two treatment modalities. Until such trials are conducted, the following are the currently accepted treatment recommendations.

The management should be guided by the degree of neurologic loss, the rapidity of onset of the neurologic symptoms, and the tumor radiosensitivity. For highly radiosensitive tumors (i.e. lymphomas, neuroblastomas), high dose steroids and radiotherapy give similar results to those obtained with decompression laminectomy (2). Our case No. 1 is a good example. We knew of the high radiosensitivity of this "thymoma" due to its rapid response to radiation in the chest. Although the diagnosis of thymoma in case No. 1 was confirmed by electron microscopy,

the course and response to radiotherapy treatment was that of a lymphoma.

There has been some controversy in the literature about "radiation induced edema" and the possibility that this may worsen the neurologic status. Very elegant studies by Rubin, et al (5) have shown in animals and clinical studies that radiotherapeutic decompression alone is adequate and achievable within hours of high dose radiation. The high dose steroids that we recommend are those we used on case No. 1, namely: Dexamethasone - 100 mg I.V. push, then 24mg I.V. Q6H x 3 days and 16mg I. V. Q6H x 2 days and 8 mg I.V. Q6H x 2 days.

The dramatic improvement of pain with high dose steroids in case No. 1 was very instructive. One can leave dye in the canal and follow the daily response to radiotherapy by fluoroscopy. Corticosteroids are effective in the prevention and transient resolution of edema (7).

Rubin et al (5) recommended high daily dose of radiation without laminectomy. The doses are 400-500r/day and when clinically improved, decrease to 150r/day. The central goal of therapy is the rapid relief of pressure in order to assure reversal or to prevent progression of the neurologic deficit.

Laminectomy should probably be reserved for patients who fail to show a rapid response to radiotherapy (as in case No. 2) or who have radioresistant tumors, and if neurologic deterioration occurs during radiotherapy. The mortality within 30 days of laminectomy is 8.7 percent (4), non-fatal complications occur in 8 percent of the cases and neurologic function deterioration as a result of surgery in 10 percent, based on a study of 226 operations done at Memorial Hospital for Cancer, N. Y. (4). It is generally agreed that decompression laminectomy should be performed in all patients with rapidly progressing or acutely severe neurologic deficits who are found by myelogram to have a



total block (2). Surgery and post-operative radiotherapy treatment is also the procedure of choice in cases of cord compression without a known 1<sup>o</sup> tumor.

Although laminectomy achieves prompt relief of cord compression, especially in tumors in the posterior compartment, it rarely results in complete removal of tumor. Radiation should be administered post-operatively. The total dose of radiation affects the outcome; suitable doses for spinal cord compression are in the range of 3,000 - 4,000 rads over 2 - 4 weeks, and depend on fractionation and tumor histology. Friedman has obtained 71 percent complete responses in lymphomas treated with 2,500 rads or above and 34 percent complete responses in patients treated with lesser doses (6).

The results of treatment of cord compression are best for lymphomas and multiple myelomas where 50 percent are ambulatory after treatment. About 1/3 of patients with breast and prostate cord compression are successfully treated.

### Prognosis

The most important prognostic indicator is the pre-treatment neurologic status. This underscores the importance of "early" detection. Sixty percent of patients who are ambulatory at the time of diagnosis remain so. Only 7 percent of patients with paraplegia at the time of diagnosis recover sufficiently to ambulate (2).

Tarlov (1) has shown in dogs, by producing spinal cord compression with a surgically implanted extradural inflatable balloon, that the reversal of the neurologic deficits produced, depended on the severity, duration, and rate of application of spinal cord pressure. With acute compression lead-

ing to paralysis recovery occurred only if the compression was relieved in two hours. If the paralysis was induced in a two-day period, it could be reversed if the compression was relieved in one week but if the cord compression was maintained for four days or longer, no recovery occurred (7). The results of therapy are better for lesions in the lower than in the upper thoracic spine.

### Conclusions

Cord compression is a serious oncologic emergency that should be suspected in any patient with malignancy and persistent back pain. Myelography should be utilized to exclude extradural spinal cord compression even in the absence of neurologic signs for an "early" diagnosis of block. Once the diagnosis is made, steroid therapy should be started. Early surgical treatment is indicated in patients with rapidly progressive neurologic deficit and complete block by myelography. If paralysis is of short duration, emergency decompressive laminectomy should be performed; if paralysis is well developed results are poor and do not justify operative morbidity and mortality.

Radiation therapy alone is an appropriate treatment for spinal cord compression in patients with minimal symptoms or metastases below the level of the conus medullaris. If the patient fails to respond rapidly, laminectomy is necessary. Successful treatment of spinal cord compression by radiation alone is most likely in radiosensitive tumors (i.e. lymphomas) and in cases of early cord compression, producing comparable results to those obtained by laminectomy and post-operative radiation.

We strongly feel that the defeatist attitude of not doing anything, due to the fact that the patient has disseminated disease and will die in a few months, should be resisted. Oncologic patients deserve preventive measures

to avoid devastating situations such as metastases of the spinal compartment produce. We have presented very clearly the excellent results obtained with "early" diagnosis of acute obstruction, and the therapeutic choices available.

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# TUBERCULOSIS: CONCEPTOS ACTUALES - PARTE I

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## Introducción

La morbilidad y mortalidad que se atribuye a la tuberculosis pulmonar en los Estados Unidos de Norte América ha disminuído dramáticamente en las últimas cuatro décadas (1). En Puerto Rico posiblemente haya ocurrido lo mismo. Esta disminución es el resultado directo de haber desarrollado quimioterapia efectiva, y ha resultado en cambios drásticos en el manejo de pacientes con tuberculosis. Se ha tratado en las últimas décadas de incluir el tratamiento de la tuberculosis dentro de la práctica de la medicina en general. Como resultado de ésto, muchos pacientes están en la actualidad siendo tratados por médicos no neumólogos. Un repaso reciente de 130 de estos pacientes demostró que más del 50 por ciento de éstos habían sido tratados inadecuadamente en alguna fase de su tratamiento antituberculoso (2). Queremos con nuestro repaso de tuberculosis en 1929 tratar de actualizar y enfatizar el impacto de la quimioterapia en el cuidado del paciente con tuberculosis pulmonar.

## La Magnitud y Espectro del Problema

A pesar de que la tasa de ataques está disminuyendo, hay más de 30,000 personas que requieren tratamiento para tuberculosis anualmente en los Estados Unidos. Los datos para Puerto Rico posiblemente sean proporcionalmente similares, más no hay evidencia directa para confirmarlo. La reactividad a tuberculina de los individuos en Estados Unidos refleja los cambios que han ocurrido en el cuadro epidemiológico de tuberculosis (3). El 7 por ciento de la población reacciona a tuberculina; de estos reactores a tuberculina, un número significativo de ellos (93 por ciento) representa personas con enfermedad activa (3).

Más del 90 por ciento de la población de los Estados Unidos de América nunca ha estado expuesta al bacilo de tuberculosis. Por lo tanto, este porcentaje de la población está a riesgo de infección. Sin embargo, este grupo a riesgo solo es responsable del 8 por ciento de la enfermedad activa.

En el pasado, el 80 por ciento de la población se infectaba durante la niñez y la prevalencia más alta de tuberculosis activa ocurría en los adultos jóvenes (4). Ese espectro ha cambiado en el momento, de tal manera que la mayor parte de los pacientes con tuberculosis tienen más de 30 años de edad (5). El haber reconocido que el espectro de la enfermedad activa está cambiando ha resultado en que las recomendaciones de tratamiento estén basadas en la patogénesis de la infección y en la respuesta inmune del anfitrión.

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## Patogénesis, Respuesta Inmunológica y Espectro Clínico

Para los propósitos clínicos, el síndrome de tuberculosis pulmonar puede ser dividido en infección primaria, enfermedad de reactivación y enfermedad diseminada o miliar.

### *Patogénesis de Tuberculosis Primaria*

La tuberculosis primaria ocurre cuando el bacilo de tuberculosis llega a una persona que no ha estado expuesta a tuberculosis anteriormente. Inicialmente, en la fase exudativa, el bacilo se multiplica libremente, los macrófagos y leucocitos polimorfonucleares migran al área y el microorganismo es fagocitado. El bacilo de tuberculosis también entra en los canales linfáticos y llega a los nódulos linfáticos regionales. La migración a la pleura durante esta fase resulta en la formación de granulomas y subsiguientemente en efusión pleural. Antes de que la multiplicación sea inhibida, hay una fase de diseminación hematógena de un número pequeño de microorganismos. Varios órganos, incluyendo el pulmón, son sembrados en esta manera y en los niños, particularmente, la tuberculosis extrapulmonar puede manifestarse. Hay un período de tiempo que ocurre entre la implantación de la lesión primaria y el desarrollo de las lesiones secundarias metastásicas. Es durante este tiempo, que la inmunidad específica se desarrolla. La respuesta inmunológica del anfitrión usualmente resulta en un nódulo fibrocaseoso calcificado, en donde permanecen los bacilos de tuberculosis atenuados. Estos lugares son el lugar de implantación primaria, los nódulos linfáticos regionales (complejo de Ghon) y los lugares metastásicos secundarios (foco de Simón) (6-8). Este tipo de inmunidad celular o hipersensitividad tardía se desarrolla

de 2 a 10 semanas después de la infección y se manifiesta por una prueba de tuberculina positiva.

### *Manifestaciones Clínicas de Tuberculosis Primaria*

Las manifestaciones clínicas de la tuberculosis primaria en adultos pueden ser agrupadas en cinco categorías (9): Estas son como siguen: 1) *conversión* de tuberculina sin enfermedad demostrable. Del 56 al 69 por ciento de las personas infectadas recuperarán sin tener evidencia radiográfica o clínica de la enfermedad. Rara vez estos individuos pueden estar levemente sintomáticos con una enfermedad del tipo neumónico (10, 11); 2) *infección simple primaria* identificada en una radiografía. El grado de enfermedad clínica varía desde un infiltrado neumónico leve con síntomas hasta el caso raro donde ocurre diseminación sistémica. La localización de las lesiones dentro del pulmón varía considerablemente. En un estudio bien documentado, todas las lesiones estaban en los segmentos anteriores del lóbulo superior o en los lóbulos inferiores o medios. Ningún caso envolvió los segmentos apicales posteriores del lóbulo superior. Adenopatía hilar está usualmente presente, y puede ser unilateral, bilateral o ipsilateral. La confirmación bacteriológica en esta situación puede esperarse en solamente 25 por ciento de los casos debido al número pequeño de microorganismos que está envuelto (12); 3) *tuberculosis primaria con efusión*. Efusión pleural puede estar presente en hasta el 30 por ciento de los pacientes con tuberculosis primaria. Un infiltrado parenquimatoso o la adenopatía asociada a la efusión está presente solamente en aproximadamente 25 por ciento de aquellos con efusiones pleurales (12). Estos pacientes tienden en promedio a presentar una enfer-

medad moderada del tipo de influenza, pero un investigador ha reportado una enfermedad aguda similar o parecida a la pulmonía bacteriana acompañada por dolor pleurítico en la mitad de los casos (11, 13). El líquido pleural es un exudado, claro en más del 80 por ciento de los casos, y serosanguinolento en menos del 10 por ciento. Los granulomas casi siempre se encuentran en una biopsia o los bacilos en el líquido pleural, en solo el 25 por ciento de los casos (13); 4) progresión a tuberculosis pulmonar crónica. Los autores escandinavos han documentado adecuadamente la progresión de la infección primaria a tuberculosis pulmonar destructiva y crónica (14, 15). La frecuencia varía con la edad, siendo más común por debajo de la edad de un año. Algunos autores han reportado una incidencia de aproximadamente un 10 por ciento (11, 14, 15) entre los adolescentes y adultos jóvenes. Todos estos pacientes están sintomáticos, de gradación moderada a severa y son usualmente clínica y radiográficamente indistinguibles de pacientes con enfermedad post-reactivación; 5) *progresión extra-pulmonar - tuberculosis miliar*. La progresión extra-pulmonar es una manifestación rara de tuberculosis primaria, que ocurre mayormente en anfitriones inmunocomprometidos.

#### *Patogénesis de la Tuberculosis Pulmonar Crónica*

La patogénesis de la tuberculosis pulmonar crónica ha sido debatida por varias décadas. Stad ha presentado evidencia convincente de que comienza como una recurrencia tardía y progresión de residuos atenuados de lesiones primarias que fueron implantados por diseminación hematógena. Esto sería mejor llamarlo reactivación en vez de reinfección. Usualmente, el lugar primario de la infección cicatriza completamente. En las áreas apicales y en los focos metastásicos (los focos de Simón), la cicatrización puede ser menos completa, ya que en

estas áreas la enfermedad está atenuada. Sin embargo, tiene el potencial de la reactivación (16-18). Hay poca evidencia en cuanto a los mecanismos de reactivación, pero se asocian condiciones tales como alcoholismo, diabetes, tratamiento con corticosteroides, silicosis y post-gastrectomía. La reactivación de la enfermedad tiende a ser limitada mayormente a los segmentos apicales y posteriores de los lóbulos superiores (85 por ciento), a los segmentos superiores de los lóbulos inferiores (9.5 por ciento) (19). La fase exudativa en la reactivación, se asocia con una infiltración polimorfonuclear leucocítica mayor que la que ocurre en enfermedad primaria y hay focos múltiples de necrosis caseosa con hemorragia e infiltración mononuclear. Estas áreas de necrosis caseosa se pueden licuar, cavitarse y vaciar al bronquio. Esta diseminación de los bacilos de tuberculosis produce sombras en otras áreas del pulmón, que pueden incluir los segmentos anteriores del lóbulo superior. En enfermedad más fulminante ocurre cuando la lesión exudativa predomina y el cuadro es uno de pulmonía tuberculosa aguda con consolidación lobar. La progresión gradual de la enfermedad con lesiones fibrosantes y pérdida de parénquima pulmonar es la forma más común de evolucionar de este tipo de condición (20).

#### *Manifestaciones Clínicas de Tuberculosis Pulmonar Crónica*

Aún en la era de la quimioterapia las manifestaciones y presentaciones clínicas de los pacientes con enfermedad de reactivación no ha cambiado. Las características de los pacientes que se presentan con enfermedad activa nos ayuda a definir el problema como existe hoy. Los síntomas clásicos e indolentes de tos, hemoptisis, fiebre, sudoración nocturna y pérdida de peso predominan. La extensión de la enfermedad es de moderada a muy avanzada en el 78 por ciento de los casos. El 72



por ciento de los pacientes son varones, 50 por ciento son alcohólicos entre las edades de cuarenta y sesenta y cuatro años y el 32 por ciento han nacido en el extranjero, fuera de los Estados Unidos de América (21). La positividad del frotis del esputo está directamente relacionada a la cantidad de enfermedad que se ve radiográficamente pero el frotis puede ser negativo hasta en el 20 por ciento de los casos que subsecuentemente tienen confirmación bacteriológica (12).

### *Respuesta Inmunológica*

La relación entre el desarrollo de hipersensitividad tardía subsiguiente a una infección primaria y la inmunidad celular sigue siendo controversial (22-25). Los eventos inmunológicos que ocurren después de una estimulación antigénica primaria son consideraciones importantes en la quimioterapia de tuberculosis pulmonar en el paciente anérgico e inmunocomprometido (26-28). Del trabajo realizado por Mackaness y otros (29), es probable que después de una infección tuberculosa los antígenos de *Mycobacterium tuberculosis* están en contacto con linfocitos B y que anticuerpos específicos a estos antígenos se formen en la superficie de estos linfocitos. Estos linfocitos están entonces inmunológicamente comprometidos con tuberculina. Cuando se re-exponen al antígeno, los linfocitos se transforman blastogénicamente y producen: 1) células citotóxicas específicas; 2) células que secretan mediadores de inmunidad celular; 3) células responsables por la memoria inmunológica. Las sustancias secretadas que median la inmunidad celular incluyen: linfotoxinas que pueden actuar directamente para destruir patógenos foráneos, el factor inhibidor de migración, el factor agregador de migración y factores quimiotácticos; todos los cuales atraen a los macrófagos a destruir el patógeno y atraen o se asocian

con la producción de factores de transferencia.

El factor de transferencia es un polipéptido con un peso molecular de menos de 10,000 que es dializable del suero. No es una inmunoglobulina y tampoco resulta inmunogénico en el recipiente, pero puede ser transferido pasivamente produciendo un estado de hipersensitividad tardía en un anfitrión no susceptible.

La administración del factor de transferencia a un anfitrión anérgico no susceptible convierte aproximadamente el 2 por ciento de la población de linfocitos a linfocitos sensitizados. En la presencia de antígenos, estos linfocitos sensitizados se dividen y proliferan. De esta manera el anfitrión adquiere hipersensitividad tardía a las proteínas de tuberculosis.

El factor de transferencia ha sido utilizado con éxito en el tratamiento de vaccinia diseminada, candidiasis diseminada, y coccidioidomicosis diseminada (29,30). El éxito del uso del factor de transferencia ha estado siempre asociado con el desarrollo de hipersensitividad tardía. Este hecho, por lo menos indirectamente, le da validez a la idea que el lograr un estado de hipersensitividad tardía es importante en la inmunidad celular adquirida o resistencia del anfitrión. La inmunocompetencia del anfitrión puede ser una consideración en la quimioterapia de tuberculosis pulmonar en situaciones especiales. Aquellos pacientes que están severamente enfermos con tuberculosis de reactivación, demuestran una respuesta linfocítica disminuida a proteínas de la tuberculina (25, 26). Si se utilizan drogas de estimulación linfocítica en pacientes anérgicos, esto puede resultar en el re-establecimiento de la hipersensitividad tardía. Whitcomb y colaboradores han reportado que el factor de transferencia fue usado exitosamente en el tratamiento de tuberculosis susceptible a drogas en un paciente que no respondió a la quimioterapia (26). La remisión de la enfermedad fue asociada con el desarrollo de



hipersensitividad tardía en el anfitrión. Toda la evidencia que se tiene sugiere que la prueba de piel con tuberculina en un paciente con enfermedad activa es útil como un indicador del pronóstico.

### *Diagnóstico de la Tuberculosis*

Las nuevas reglas en el diagnóstico de la tuberculosis se basan en la patogénesis de la enfermedad y en la relación entre anfitrión y parásito. Los términos activo, inactivo, mínimo, moderado y avanzado no se utilizan más. Estos términos fueron índices útiles de pronóstico antes de la era de la quimioterapia; hoy, un curso apropiado de quimioterapia determinará el pronóstico excepto en situaciones muy especiales. La nueva clasificación refleja una predicción de Robert Kock en 1882: "In the future it will not be difficult to decide what is tuberculosis and what is not... the demonstration of tubercule bacilli....will settle" (32). La determinación de la etapa de tuberculosis se basa en la actualidad: en exposición a tuberculosis, la prueba de piel de tuberculina, y la confirmación bacteriológica. La exposición a tuberculosis continúa siendo un dato histórico y la confirmación bacteriológica puede hacerse en laboratorios de referencia y en algunos laboratorios generales, más desafortunadamente en Puerto Rico la confirmación bacteriológica se limita en la actualidad a uno o dos laboratorios en la isla. Ya que la infección, y posiblemente el pronóstico, se basa en la prueba de piel de tuberculina, hay que hacer ciertas recomendaciones especiales.

Se acepta generalmente que la prueba intradérmica debe de hacerse utilizando el antígeno PPD-S. Este antígeno está estabilizado con Tween 80 y ha demostrado tener la incidencia más baja de falsos negativos cuando se administra a pacientes que tienen tuberculosis documentada bacteriológicamente (33). Si los

errores técnicos se eliminan, la evidencia indica que la incidencia de falsos negativos es alrededor de 20 por ciento (33-35). Los no reactores al antígeno PPD-S con tuberculosis pulmonar documentada bacteriológicamente han sido investigados y se ha encontrado que estas personas son las que están seriamente enfermas clínicamente, y en las cuales usualmente la albúmina sérica es menor de tres gramos. Cuando a este grupo de personas se le repite la prueba después de dos semanas de tratamiento antituberculoso con un régimen nutricional adecuado, una reacción positiva se obtiene en el 94 por ciento de esta población (34). Estudios demuestran que el uso de las pruebas de piel con PPD-S (5TU) son un índice sensitivo de infección cuando se está tratando de determinar el status del paciente con tuberculosis. El uso de PPD de concentración mayor (250 TU) no ha sido evaluado con el antígeno estabilizado y su utilidad clínica es impredecible.

### *Quimioterapia de Tuberculosis Pulmonar*

#### *Clasificación*

La recomendación para la quimioterapia de tuberculosis pulmonar se puede dividir en la actualidad en cuatro categorías basadas en las reglas revisadas para diagnóstico. a) *grupo O: pacientes sin exposición no infectados* (PPD-negativo). No se requiere acción médica en relación a tuberculosis; b) *grupo I: exposición a tuberculosis; sin evidencia de infección - (PPD- negativo)*. Si la exposición ha sido remota no se requiere ninguna acción. Si la exposición ha ocurrido en los tres meses previos, una prueba de PPD-S debe de repetirse tres meses después de que la exposición ha terminado. Si la prueba PPD-S es positiva entonces el paciente cae en el grupo II y debe ser tratado; c) *grupo II: pacientes infectados sin enfermedad*. El tratamiento de individuos que están infecta-

dos sin enfermedad evitara el 90 por ciento de los 30,000 nuevos casos de tuberculosis que ocurren cada año (3). Se estima que cada nuevo caso produce infección en dos a tres individuos previamente no infectados, la quimioterapia de este grupo virtualmente podría erradicar tuberculosis como un problema de salud pública (36).

En esta población infestada el riesgo para desarrollar tuberculosis debe ser pesado en contra del riesgo de desarrollar hepatitis por isoniácida cuando se recomienda profilaxis. El riesgo de desarrollar tuberculosis durante la vida de una persona que tiene un PPD-S de más de 10 milímetros en un momento dado, puede calcularse. El riesgo disminuye con la edad, de aproximadamente 4.5 por mil a la edad de 25 años a 1.5 por mil a la edad de 65 (37).

El tratamiento con isoniácida resulta en una reducción en el riesgo de tuberculosis a través de la vida de tal manera que el número de casos de tuberculosis que se previenen por isoniácida puede ser calculado (37). Por ejemplo, a la edad de 25 años un paciente con un PPD positivo de más de 10 milímetros, el cual recibe isoniácida, tiene una posibilidad de prevención de 3.2 por mil, mientras que a la edad de 65 años la posibilidad de prevención es de 0.9 por mil (38).

La incidencia de hepatitis asociada a la administración de isoniácida en personas de más de 20 años de edad ha sido revisada en un estudio de más de 11,000 personas recibiendo profilaxis y los resultados son como sigue (39): en personas de 25 años de edad, el estimado de riesgo de desarrollar hepatitis al recibir isoniácida es de 0.6 por mil; a los 35, de 1.3 por mil; a los 53, de 2.0 por mil; y los 65, de 2.6 por mil. De estos datos puede calcularse que el riesgo de desarrollar hepatitis durante un año de tratamiento con isoniácida varía desde 2.4 por mil entre los adultos de menos de 35 años de edad a 19 por mil en personas entre las eda-

des de 55 a 64 años de edad (38, 39).

Debido a que estos datos claramente indican que existe un riesgo de hepatitis relacionada con la edad, es necesario identificar los individuos que están a un riesgo aún mayor para desarrollar tuberculosis pulmonar. En ciertos grupos de personas se ha demostrado una tendencia mayor a desarrollar tuberculosis pulmonar y sus características han sido definidas (40). Entre estos, se encuentran los pacientes que han convertido a positiva la prueba de tuberculina recientemente. Estos pacientes durante el primer año de conversión tienen un riesgo de cinco a quince por ciento, después del primer año de conversión el riesgo baja a 3.5 por ciento. Aquellas personas que han estado en contacto con casos nuevos de tuberculosis y que tienen un PPD positivo al hacer la prueba de tuberculosis tienen un riesgo de 5 por ciento; si la prueba de PPD es negativa el riesgo se disminuye a la mitad. Aquellos pacientes que tienen un PPD de más de 10 milímetros de induración con una radiografía de pecho anormal, tienen un riesgo de 1 a 5 por ciento por año. Aquellos que tienen tuberculosis que no ha sido bien tratada tienen un riesgo de 1.3 por ciento por año y aquellos adultos con tuberculina positiva con radiografía de pecho normal tienen un riesgo de 0.08 por ciento por año. Los riesgos relativos han llevado a las siguientes recomendaciones para el uso quimoprofiláctico de isoniácida, esto es 300 mg al día por el período de un año (40). Se recomienda profilaxis con isoniácida para personas que han convertido recientemente a la prueba de piel con PPD; para personas que son contactos en la casa de casos nuevos de tuberculosis; para personas que tienen enfermedad que no ha sido tratada adecuadamente; para personas con un PPD positivo y una radiografía de pecho anormal, para niños y adolescentes con PPD positivo aunque tengan una radiografía de pecho normal.

Hay evidencia menos convincente sobre los riesgos de desarrollar tuberculosis clínica con la



prueba de tuberculina positiva en otras situaciones específicas. Los siguientes grupos deben incluirse, según las recomendaciones de la American Thoracic Society (40): aquellos pacientes que estén recibiendo tratamiento prolongado con adrenocorticosteroides, pacientes en tratamiento inmunosupresivo, pacientes con malignidades hematológicas y reticuloendoteliales, pacientes con diabetes mellitus, con silicosis y postgastrectomía deben de recibir profilaxis. No hay evidencia de que continuar quimioprofilaxis por más de un año en estas situaciones sea beneficioso. Si estos criterios para quimioprofilaxis se siguieran estrictamente por todos los médicos y oficiales de salubridad pública se disminuirían significativamente los nuevos casos de tuberculosis. d) *grupo III: infectados con enfermedad*. Todo paciente con enfermedad de tuberculosis debe de recibir un curso adecuado de quimioterapia. Una serie de numerosos estudios bien controlados ha documentado que el descanso, dieta, clima y factores psicológicos no tienen influencia en el curso de la enfermedad o en el número de recaídas (41, 46). Aún más, se ha demostrado recientemente que cuando los resultados de quimioterapia en el tratamiento inicial se combinan con los resultados de retratamiento, el por ciento de pacientes que se espera tengan recaída se aproxima al 0.05 por ciento (47, 48).

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## EFFECT OF ORAL CONTRACEPTIVE ON HEMATOCRIT LEVEL

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**Summary:** A study has been made of 7,720 women from the Maternal Health Program at the University of Puerto Rico School of Medicine with the purpose of examining the significance of a high dosage oral contraceptive on hemoglobin concentration. The subjects in the experiment were almost equally distributed in two groups through a randomization process: 3,839 (49.7 percent) for the oral contraceptive group and 3,881 (50.3 percent) for the non-oral group. The study revealed that the mean hematocrit level (measured according to micro-hematocrit test) of the oral group was 36.57 percent ml., with a standard deviation of 3.74 while that of the vaginal group was 36.63 percent ml., with a standard deviation of 3.69. Statistically, there was no significant difference between the two mean hematocrit levels. It was also observed from the statistical analysis that the percentage frequency distributions of the hematocrit level of the two groups of patients did not differ from each other. No definite trend in hematocrit level was noted according to differences in ages nor in the number of medical cycles.

### Introduction

The control of fertility with oral contraceptives has had a great public acceptance since the first field trial in Puerto Rico in 1956. After all these years of continuous use it is now recognized as the most effective method of voluntary family planning.

Some of the most common side effects of oral hormonal contraceptives are spotting, breakthrough-bleeding nausea, vomiting, breast tenderness and weight gain, but most of these symptoms diminish with successive cycles and can also be minimized by a correct adjustment of dosage or shift in the content of the estrogen-progesterone combination.

No changes in the hematic nor on blood viscosity picture were seen as exclusively related to the use of oral contraceptives (1,5). Very few articles on this subject have been published in scientific journals. Pincus et al report that no significant differences in hemoglobin levels were noted during or after medication as compared with those of untreated women (4). Burton (3) shows in his work that the mean hemoglobin level was slightly higher in groups taking oral contraceptives, though the difference was not statistically significant.

In the present report an attempt is made by us to examine the significance of the effects of a high dosage oral combination of a pro-

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*Appreciation is expressed to G. D. Searle and Co. for supplying Enovid.*

**TABLE I**  
**Number and Percentage of Women Assigned to Two Groups**  
**By Year of Admission**

<i>Year of Admission</i>	<i>Oral (OCG)</i>		<i>Vaginal (VCG)</i>		<i>Both Groups</i>	
	<i>Number</i>	<i>Percent</i>	<i>Number</i>	<i>Percent</i>	<i>Number</i>	<i>Percent</i>
1961	46	48.9	48	51.1	94	100.0
1962	502	48.3	537	51.7	1,039	100.0
1963	507	49.4	519	50.6	1,026	100.0
1964	1,005	49.6	1,021	50.4	2,026	100.0
1965	940	49.8	947	50.2	1,887	100.0
1966	776	49.8	781	50.2	1,557	100.0
1967	817	49.7	827	50.3	1,644	100.0
1968	205	49.9	206	50.1	411	100.0
<i>All Years</i>	4,798	49.6	4,886	50.4	9,684	100.0

gestational substance with ethinyl estradiol\* on hemoglobin concentration.

### Material and Method

During the period between 1961 and 1968, 9,684 women were admitted to the Maternal Health Study at the University of Puerto Rico School of Medicine. These women were randomly assigned one of the two contraceptive methods: about half of them (4,798 or 49.6 percent) fell into the oral contraceptive group (OCG) that used a combination contraceptive pill and the rest (4,886 or 50.4 percent) into the va-

ginal or non-oral contraceptive group (VCG) who used a vaginal contraceptive method excluding any form of intrauterine device. Table I shows the distribution of the women by year of their admission to the two groups of the experiment. This table shows that the randomization process was successful in that the assignment of the two kinds of treatment distributed the patients in a similar manner within each year. The average age was 28.3 years for the OCG and 28.9 for the VCG; the median years for the two groups, were 27.7 and 28.3 years respectively. In a related paper published by Fuertes and Bangdiwala (6), the procedure of randomization has been described in details wherein it has been shown through appropriate statistical analysis that the two groups, oral and vaginal, are fairly well matched in a number of basic characteristics and hence are considered to be directly comparable for the purpose of analysis of various other parameters in the two groups.

Before therapy was started each patient under-

\* The oral contraceptive group used norethynodrel, 5 mg. and mestranol, 0.075 mg. (Enovid, G. D. Searle Co. The total steroid dosage was 5.95 mg. for tablet).



TABLE II

Distribution of Hematocrit Level in Percent for Oral (OCG)  
(First - Initial Visit) and Vaginal (VCG) Groups

Hematocrit Percent	Oral Group (OCG) (n = 3839)		Vaginal Group (VCG) (n = 3881)	
	Relative Percent	Cumulative Percent	Relative Percent	Cumulative Percent
Less than 29.6	3.2	3.2	2.8	2.8
29.6 - 30.5	2.7	5.9	2.8	5.6
30.6 - 31.5	2.1	8.0	2.1	7.7
31.6 - 32.5	4.3	12.3	3.7	11.4
32.6 - 33.5	5.1	17.4	5.5	16.9
33.6 - 34.5	7.4	24.8	8.1	25.0
34.6 - 35.5	12.3	37.1	12.1	37.1
35.6 - 36.5	12.3	49.4	11.2	48.3
36.6 - 37.5	11.5	60.9	12.0	60.3
37.6 - 38.5	11.1	72.0	11.1	71.4
38.6 - 39.5	7.5	79.5	8.4	79.8
39.6 - 40.5	8.5	88.0	8.2	88.0
40.6 - 41.5	3.9	91.8	3.9	91.9
41.6 - 42.5	3.5	95.4	3.5	95.4
42.6 and More	4.6	100.0	4.6	100.0
	100.0		100.0	

went a routine physical examination and a careful history was obtained. At the beginning and at each annual physical examination thereafter special attention was given to weight, blood pressure, urinalysis, cervical cytology study and hematocrit. Each patient returned every two months for a new supply of the contraceptive assigned and for updating of the health data record. If the physical examination or the laboratory data disclosed any abnormality, the patient was examined more frequently.

The hematocrit values were obtained according to the microhematocrit test. Two hematocrit capillary tubes were filled to within 1/4 inch of the upper end of the tube with blood specimen obtained by

puncturing of the index finger. The tubes were then sealed with plasticene, and centrifuged (International Model M. B.) for 5 minutes. Both specimens were read independently to the nearest percent hematocrit level directly from an international Micro-capillary Reader, Model CK. The two values obtained for each examinee were averaged. The mean value was recorded as the individual's hematocrit in percent milliliter units.

*Hematocrit Reading for Oral and Vaginal Groups Comparison by Number of Cycles*

Of the 9,684 total number of patients in the

TABLE III

Mean and Median Hematocrit Levels for Oral (OCG)  
and Vaginal (VCG) Groups

	<i>Oral Group (OCG)</i>	<i>Vaginal Group (VCG)</i>
<i>Number of Women</i>	<i>(3889)</i>	<i>(3881)</i>
<i>Mean Hematocrit Level</i>	<i>36.57 Percent</i>	<i>36.63 Percent</i>
<i>Median Hematocrit Level</i>	<i>36.56 Percent</i>	<i>36.65 Percent</i>
<i>Standard Deviation</i>	<i>3.74</i>	<i>3.69</i>

study, the hematocrit readings were available for a total of 7,720 (79.7 percent) patients. At the time of their first or initial visit the patients were almost equally represented by both the OCG and VCG groups: 3,839 (80.0 percent of the 4,798) for the oral group (OCG) and 3,881 (79.4 percent of the 4,886) of the vaginal group (VCG).

The distribution (in percent) of the hematocrit level of the study patients for both groups at the first (initial) visit is given in Table II. The difference between the two distributions, as can be seen from the table (and as tested by Chi-square statistic) is not significant. There were almost equal number of women with the same hematocrit level in both groups: for example, about one fourth of the subjects in both groups have hematocrit below 34.5 percent, and another one fourth above 39.0 percent.

The mean hematocrit level of the oral (OCG) group was 36.57 percent with a standard deviation of 3.74 percent while that of the vaginal (VCG) group was 36.63, with a standard deviation of 3.69. Statistically, there is no significant difference between the two averages. The medians too, in both cases, almost

coincide. (Table III).

Hematocrit level was measured also for women during their:

- (a) second visit and had 1 to 4 medical cycles
- (b) second visit and had 5 or more cycles.
- (c) third visit and had 11 or more cycles.
- (d) fourth visit and had 21 or more cycles.
- (e) fifth visit and had 28 or more cycles.

On analyzing the data for the distribution of hematocrit level at each visit, there were no remarkable differences observed ( $\chi^2$  value not significant at 5 percent level) between the oral and vaginal group women.

Within each group (OCG and VCG), the tendency is to have less proportion of women having lower hematocrit level with increasing number of cycles; that is, on an average the hematocrit level is increasing very slightly with higher number of medical cycles, as can be seen from Table IV, where the averages of percent hematocrit are compared at different cycles. At none of the periods of different cycles, however, did the average hematocrit level differ significantly between the OCG and VCG. It may be noted that the average

TABLE IV  
Mean Hematocrit Level (in Percent) for OCG and  
VCG at different periods (Medical Cycles)

Visit Number	Number of Cycles	Number of Women	ORAL (OCG)		Number of Women	VAGINAL (VCG)		Dif- ference
			Mean	S.D.		Mean	S.D.	
Initial	Zero	(3,839)	36.57	3.74	(3,881)	36.63	3.69	NS
Second	1 - 4	(677)	36.09	4.13	(437)	35.94	4.31	NS
Second	5 or more	(1,798)	36.38	3.70	(1,627)	36.23	4.05	NS
Third	11 or more	(1,386)	36.52	3.51	(1,183)	36.74	3.90	NS
Fourth	21 or more	(846)	36.73	3.47	(648)	36.91	3.78	NS
Fifth	29 or more	(542)	36.90	3.19	(368)	37.51	3.57	NS

NS = Difference between two means is not significant at 5 percent probability level.

level tends to increase with the number of cycles in both groups, after going down slightly from the initial visit up to the next visit. At the initial visit for OCG group, the mean was 36.57; it went down to 36.09 at the next visit up to 4 cycles but thereafter it started increasing again. In the VCG group, the mean hematocrit was 36.63 at the initial visit which decreased to 35.94 for the group which made the second visit and had less than 5 cycles, but the level increased thereafter, just as in the case of the OCG group.

For the purpose of reference some selected percentile values of the hematocrit level by cycles are calculated and presented in Table V.

#### Comparison by Age Groups

In this section, comparison is made for each group of women - Oral and Vaginal Contraceptive Groups - of the hematocrit levels between the two groups belonging to the same age grouping.

The average hematocrit level at the first (initial) visit for the group of 21-25 years of age was found to be 36.67 percent in the OCG group compared with 36.53 for the VCG group. The difference, however, is not significant statistically. Table VI presents averages for different age groups; none of the differences are significant. Also, there is no increasing nor decreasing tendency due to change in age group noticed in the mean hematocrit level. The distributions of hematocrit level for selected percentile points by age groups are given in Table VII. No significant differences were observed between the distributions of OCG and VCG.

The statistical analysis showed also that the average value of the hematocrit level of the OCG for different age groups at successive visits, after the initial one, did not differ significantly from the corresponding average of the women of the VCG group.

#### Discussion

We might have to think that the constant



TABLE V

Hematocrit in Percent by Number of Cycles for Selected Percentiles  
for Oral (OCG) and Non-Oral (VCG) Groups

No. of Cycles	Zero		1-4		5-10		11-20		21-28		29 or More	
	OCG	VCG	OCG	OVCG	OCG	VCG	OCG	VCG	OCG	VCG	OCG	VCG
Percentile												
99	46.4	46.4	46.3	46.4	46.3	46.4	46.1	46.6	46.3	46.4	46.1	46.8
97.5	44.8	44.8	44.5	44.6	44.6	44.7	44.0	45.4	44.5	44.8	43.9	45.8
95	42.4	42.4	42.2	42.3	42.3	42.3	42.1	43.2	42.3	42.4	42.1	44.1
90	41.0	41.0	40.9	40.8	40.8	41.0	40.8	41.3	40.8	41.3	40.8	42.0
80	39.6	39.5	39.3	39.3	39.3	39.4	39.2	39.7	39.6	39.8	39.4	40.4
75(Q <sub>3</sub> )	38.9	38.9	38.6	38.7	38.5	38.7	38.7	39.1	39.0	39.2	39.0	39.6
70	38.4	38.4	38.1	38.1	38.0	38.1	38.2	38.6	38.5	38.8	38.5	39.1
60	37.4	37.5	37.2	37.1	37.1	37.2	37.3	37.6	37.5	38.0	37.7	38.1
50(Med)	36.6	36.7	36.3	36.1	36.3	36.3	36.5	36.8	36.7	37.1	36.9	37.3
40	35.7	35.8	35.4	35.1	35.5	35.4	35.7	35.9	35.8	36.3	36.0	36.7
30	34.9	34.9	34.4	34.2	34.7	34.6	34.9	35.1	35.0	35.4	35.2	35.8
25(Q <sub>1</sub> )	34.5	34.5	33.8	33.8	34.2	34.1	34.5	34.6	34.6	34.9	34.7	35.3
20	33.8	33.9	33.1	33.1	33.7	33.4	33.9	33.9	34.1	34.2	34.2	34.7
10	32.0	32.1	31.5	31.3	32.3	31.6	32.5	32.2	32.6	32.2	32.9	33.1
5	30.2	30.3	29.8	29.0	30.7	29.9	31.0	30.5	31.4	30.4	31.7	31.6
2.5	28.8	29.1	25.5	24.3	29.6	26.2	29.9	28.3	30.2	28.1	30.7	30.5
1	26.5	26.9	21.9	21.4	24.5	22.8	25.9	24.2	27.1	25.4	29.8	29.0

Q<sub>1</sub> = Lower quartile, Q<sub>3</sub> = Upper quartile, Med = Median

menstrual flow may easily induce a state of iron deficiency markedly in a population like ours with a low iron in-take and a low hemoglobin. It is suggested that negative iron balance might be improved by reduction of menstrual flow

as a result of the use of oral contraceptive steroids.

We have studied 7,720 hematocrit readings, almost equally distributed in both the oral and non-oral contraceptive users. The study re-

TABLE VI

Mean and Median Hematocrit Levels (In Percent) for Oral (OCG)  
and Vaginal (VCG) Groups by Age (Initial Visit - Zero Cycles)

	21-25		26-30		31-35		36-40	
	OCG	VCG	OCG	VCG	OCG	VCG	OCG	VCG
<i>Number of</i>								
<i>Women</i>	(1,352)	(1,192)	(1,443)	(1,448)	(674)	(777)	(370)	(464)
<i>Mean Hematocrit</i>								
<i>(Percent)</i>	36.67	36.53	36.57	36.66	36.61	36.76	36.16	36.55
<i>Median Hemato-</i>								
<i>crit (Percent)</i>	36.62	36.59	36.54	36.61	36.59	36.85	36.21	36.60
<i>Standard</i>								
<i>Deviation</i>	3.58	3.49	3.75	3.72	3.84	3.81	4.09	3.87

vealed that the hematocrit levels of both groups were similar at different periods of medical cycles. These findings are in accordance with those reported by Dr. Gregory Pincus when he started with this group in 1958 and also with those of studies by Rice Wray (12) in 1962 and later, also by Burton (3) in Great Britain, who found a slightly higher hemoglobin level in the group taking oral contraceptive, though the difference was not statistically significant.

Alterations in the metabolism of certain vitamins and minerals in women who use oral contraceptive steroids have been reported by many authors (7,8).

Thever R. C. and Briggs (7, 8) indicate in their works that the requirements for vitamin B<sub>6</sub> (Pyridoxine) by women using oral contraceptive is higher. They also report folic acid deficiency in those women, as well as an apparent increase of vitamin C. Wortalik and associates (9) and Davis and Smith (10) observed a reduction in vitamin B<sub>12</sub> levels in oral contraceptive consumers.

On the other hand Prasad et al (11) observed a relatively deficient state with respect to vitamin B<sub>6</sub> and folic acid in contraceptive users, but no significant effects on serum vitamin B<sub>12</sub> was observed by them as a result of oral contraceptive administration.

TABLE VII

Hematocrit in Percent by Age Group for Selected Percentiles for  
Oral (OCG) and Non-Oral (VCG) Groups - Initial Visit (Zero Cycles)

Age Group	21-25		26-30		31-35		36-40	
	OCG	VCG	OCG	VCG	OCG	VCG	OCG	VCG
Percentile								
99	46.2	45.6	46.5	46.6	46.5	46.6	46.5	46.4
97.5	44.3	43.4	45.0	45.2	45.1	45.3	44.8	44.8
95	42.2	41.9	42.5	42.9	42.8	43.1	42.4	42.4
90	40.9	40.7	41.0	41.2	41.3	41.5	41.0	40.9
80	39.5	39.3	39.6	39.5	39.6	39.7	39.6	39.8
75 ( $Q_3$ )	38.9	38.7	39.3	38.9	38.9	39.1	38.9	39.3
70	38.3	38.2	38.3	38.4	38.4	38.5	38.3	38.7
60	37.4	37.4	37.5	37.4	37.5	37.7	37.2	37.5
50 (Med)	36.6	36.6	36.5	36.6	36.6	36.9	36.2	36.6
40	35.9	35.8	35.7	35.7	35.8	35.8	35.3	35.7
30	35.1	35.0	34.9	34.9	34.9	34.9	34.4	34.8
25 ( $Q_1$ )	34.7	34.6	34.5	34.5	34.4	34.5	33.7	34.2
20	34.2	34.0	33.8	33.9	33.7	33.9	32.8	33.5
10	32.4	32.5	32.0	32.2	31.9	31.9	31.1	31.4
5	30.4	30.4	30.4	30.5	29.9	30.2	29.5	29.8
2.5	29.1	28.8	28.9	29.6	28.8	29.3	27.8	28.8
1	27.2	26.9	26.0	26.6	27.6	27.4	25.9	26.8

$Q_1$  = Lower quartile,  $Q_3$  = Upper quartile, Med = Median

We can conclude that our data demonstrate that oral contraceptive steroids do not affect the level of hemoglobin in blood in those women who use it irrespective of the length of time used.

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—CONTESTACIONES—

1. B
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3. CIERTO
4. FALSO
5. FALSO
6. C
7. D
8. D
9. FALSO
10. D

# CARDIAC PACEMAKERS AND PREGNANCY

## A FOLLOW-UP AND ANNOTATION

Charles D. Johnson, MD

**Summary:** A follow-up and annotation of the subsequent pertinent medical literature is made of a previously reported 24-year-old female with heart block and a permanent epicardial pacemaker. She has now completed two uneventful and uncomplicated pregnancies (including labor and delivery), supporting the value of cardiac pacemakers in pregnant patients with heart block.

**Resumen:** Se hace anotaciones sobre literatura médica pertinente y datos de seguimiento en una mujer de 24 años con bloqueo cardíaco y un marcapaso epicárdico permanente previamente reportado. Ella ha completado 2 embarazos normales sin complicaciones (incluyendo parto y alumbramiento), respaldando el valor de los marcapasos cardíacos en mujeres embarazadas con bloqueo cardíaco.

Uneventful pregnancy, labor and delivery in a young female with complete heart block and a permanent epicardial demand pacemaker was reported in this journal in 1977 (1). As far as

was known she represented the first such case in Puerto Rico. A review was made of the small number of other such documented cases from the medical literature. The generally rewarding value of pacemakers in these patients was emphasized.

### A Follow-up

The patient continued to do well and was followed in our Cardiac Clinic. Contraceptive measures (coil) were practiced for a period of time. On May 9, 1978 the pacemaker generator was replaced with a new Medtronic lithium unit, Model 5973, and the rate set at 72 impulses per minute. Her cardiac status remained stable. She became pregnant again in 1978 (age 23 yrs). The prenatal period was, in general, uncomplicated. The pacemaker continued to sense, and pace at a rate of 72 while the atrial rhythm was sinus at approximately 90/min. Gestation was term and labor spontaneous. A pulse of 80 was recorded. P waves were prominent; paced and fusion beats were observed. Monitored fetal heart rate was normal. Labor, vaginal delivery (semi-sitting position) and the postpartum period were uneventful and the baby normal. Low forceps (Simpson), local anesthesia and Ringer's lactate were used, but no oxytocin or other drugs were administered.

The initial cardiac pacemaker was

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*From the University of Puerto Rico School of Medicine, Department of Medicine, Section of Cardiology Río Piedras, Puerto Rico 00936.*

placed in this patient at age 16 yrs. 4 yrs prior to her first pregnancy, because of symptoms of heart block, with Stokes-Adams attack and brady-arrhythmia. The etiology of her heart block was unknown but is considered to be due to congenital atrioventricular (AV) block or to a viral myocarditis. Electrocardiograms showed right axis deviation, right bundle branch block, first degree, 2:1 and advanced second degree, and complete AV block, etc..

### Annotation

Since the previous literature review 3 other cases of pregnancy and complete heart block have come to attention, it being stated that the literature contains over 100 successful deliveries in patients with complete heart block (2).

A 20-year-old (3) with asymptomatic congenital complete heart block developed multiple Stokes-Adams seizures starting with pregnancy (pulse 50/min). She was observed for 2 months and when pregnancy reached 26 weeks, an epicardial Medtronic pacemaker was implanted (rate 80) via anterior thoracotomy. At full term she underwent a normal spontaneous delivery of a normal baby. She later delivered a second normal baby 36 months after implantation of the pacemaker.

Eddy & Frankenfeld (2) added 2 cases. The first was a 21-year-old primipara with an otherwise normal heart (normal QRS contour, ventricular rate 32) who delivered uneventfully (aided by oxytocin, low forceps and saddle block anesthesia), but who required a permanent pacemaker a year later because of the development of syncope. The second was a 21-year-old

primipara with a slow heart rate since birth believed to have a congenital myocardiopathy, who possessed a previous functioning permanent pacemaker (Ventricor). Vaginal delivery was attempted but failed. Immediately following cesarean section (viable infant), the patient developed severe pulmonary edema attributed to the work of delivery, increased plasma volume and intravenous infusion overload, general anesthesia, the fixed ventricular rate, lack of atrial kick and weakened left ventricle from the myocardiopathy. Medical therapy was successful. The authors recognized that an increased stroke volume in the setting of a slow heart rate may provide the higher cardiac output for the demands of labor. But occasionally, syncope and convulsions may complicate labor, caused by heart slowing during a Valsalva maneuver, for which insertion of a temporary transvenous pacer just prior to delivery is indicated. Continuous cardiac monitoring during labor and the puerperium should be practiced and a temporary pacemaker be made available for syncope or excessive slowing. If underlying heart disease exists they believe that pacemaker placement at the onset of labor should be considered, as well as the avoidance of fluid overload and treatment of heart failure. They too found that block due to acquired heart disease carried a greater risk than that secondary to congenital disease (2).

### Acknowledgment

University Hospital Obstetrics Department for their role in the management of this patient.



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## LA IMPORTANCIA DE LOS SERVICIOS DE REHABILITACION EN UN HOSPITAL GENERAL

*Según la ciencia médica ha ido conquistando las enfermedades, así también ha multiplicado las complicaciones de la vida. El hombre vive ahora doble la edad de su bisabuelo. Nuestros hospitales se están llenando lentamente de ancianos, pacientes crónicos y niños y adultos incapacitados. El "Staff" médico no se interesa mayormente por el paciente con un diagnóstico tan poco exitante como hemiplegia, artritis degenerativa o perlesía cerebral. La admisión de un caso de mielitis transversa con su resultante paraplegia trae a la mente del médico residente la inevitable complicación de úlceras de decúbito y muerte como una bendición secundaria a fallo renal después de un período de hospitalización prolongado ocupando una cama necesitada para otros pacientes.*

*Hoy en día, a medida que aumenta la longevidad, el hospital para enfermedades agudas es mal llamado. Un cuarenta por ciento de las camas de nuestros hospitales generales están ocupadas por ancianos, enfermos crónicos y niños y adultos incapacitados. Es precisamente para el tratamiento de este creciente tipo de pacientes que es necesario un programa efectivo de medicina física y rehabilitación en cada hospital general. Este gran grupo de pacientes requiere cuido individual por un período más prolongado que cualquier otro y el costo de hospitalización es escalofriante.*

*Si son devueltos sin tratamientos a su hogar, el costo al gobierno en términos de bienestar público, en los ahorros de la familia y el tiempo invertido en cuidarlos es fantástico. Cuanto mejor sería para todos si se les brindase la oportunidad de regresar a una vida productiva o por lo menos una autosuficiente, social y económicamente. Ningún miembro del personal médico del hospital, una vez que se le hayan explicado claramente los beneficios de rehabilitación, podría negar esta necesidad. Ningún estado, una vez entienda la economía en dinero y brazos, podría negarse a beneficiarse de la organización de un centro completo de rehabilitación.*

*Un programa de esta naturaleza dentro de un hospital general debe incluir un servicio de medicina física y rehabilitación y una sala o varias camas para rehabilitación. No es suficiente que los pacientes sean referidos para tratamiento con alguna modalidad física. Debe haber una sala de rehabilitación a donde el médico y el cirujano puedan referir o trasladar sus pacientes como preparativo para alta de hospital una vez terminado su tratamiento. Al removerse estos pacientes de las*

*salas de casos agudos, le permite al personal médico dedicar todo su tiempo a aquellos casos que más lo requieran sin tener que ocuparse de largas convalecencias, pacientes crónicos, ancianos, o incapacitados. Esta clase de programa significa la continuidad del excelente cuidado moderno, diagnóstico y tratamiento definitivo incluyendo la rehabilitación, o el retorno del paciente a su hogar y a su comunidad en el mejor estado físico, mental, social y económico posible.*

*La medicina física y rehabilitación ofrece las formas o instrumentos más antiguos conocidos en la medicina para tratamiento. Sin embargo, ofrece la manera más sistemática de un tratamiento completo. Además reduce materialmente los costos de funcionamiento del hospital y mantenimiento de los pacientes en la casa.*

Herman J. Flax, MD, FACP





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\*This drug has been classified "probably" effective in treating functional bowel/irritable bowel syndrome.

†See Warnings, Precautions and Adverse Reactions.

See following page for prescribing information.

Reference:

King, J.C. and Starkman, N.M.: Evaluation of an antispasmodic. Double-blind evaluation to control gastrointestinal spasms occurring during radiographic examination. A preliminary report. Western Med. 5:356-358, 1964.

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Brief Summary

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For use in the treatment of infant colic (syrup).

Final classification of the less-than-effective indications requires further investigation.

**CONTRAINDICATIONS:** Obstructive uropathy (for example, bladder neck obstruction due to prostatic hypertrophy); obstructive disease of the gastrointestinal tract (as in achalasia, pyloroduodenal stenosis); paralytic ileus, intestinal atony of the elderly or debilitated patient, unstable cardiovascular status in acute hemorrhage, severe ulcerative colitis, toxic megacolon complicating ulcerative colitis, myasthenia gravis. **WARNINGS:** In the presence of a high environmental temperature, heat prostration can occur with drug use (fever and heat stroke due to decreased sweating). Diarrhea may be an early symptom of incomplete intestinal obstruction, especially in patients with ileostomy or colostomy. In this instance treatment with this drug would be inappropriate and possibly harmful. Bentyl may produce drowsiness or blurred vision. In this event, the patient should be warned not to engage in activities requiring mental alertness such as operating a motor vehicle or other machinery or perform hazardous work while taking this drug. **PRECAUTIONS:** Although studies have failed to demonstrate adverse effects of dicyclomine hydrochloride in glaucoma or in patients with prostatic hypertrophy, it should be prescribed with caution in patients known to have or suspected of having glaucoma or prostatic hypertrophy. Use with caution in patients with Autonomic neuropathy. Hepatic or renal disease. Ulcerative colitis. Large doses may suppress intestinal motility to the point of producing a paralytic ileus and the use of this drug may precipitate or aggravate the serious complication of toxic megacolon. Hyperthyroidism, coronary heart disease, congestive heart failure, cardiac arrhythmias, and hypertension. Hiatal hernia associated with reflux esophagitis since anticholinergic drugs may aggravate this condition.

Do not rely on the use of the drug in the presence of complication of biliary tract disease. Investigate any tachycardia before giving anticholinergic (atropine-like) drugs since they may increase the heart rate. With overdosage, a curare-like action may occur. **ADVERSE REACTIONS:** Anticholinergics/antispasmodics produce certain effects which may be physiologic or toxic depending upon the individual patient's response. The physician must delineate these. Adverse reactions may include xerostomia, urinary hesitancy and retention; blurred vision and tachycardia; palpitations; mydriasis; cycloplegia; increased ocular tension; loss of taste; headache; nervousness; drowsiness; weakness; dizziness; insomnia; nausea; vomiting; impotence; suppression of lactation; constipation; bloated feeling; severe allergic reaction or drug idiosyncrasies including anaphylaxis, urticaria and other dermal manifestations; some degree of mental confusion and/or excitement, especially in elderly persons; and decreased sweating. With the injectable form there may be a temporary sensation of lightheadedness and occasionally local irritation. **DOSE AND ADMINISTRATION:** Dosage must be adjusted to individual patient's needs.

**Usual Dosage:** Bentyl 10 mg, capsule and syrup: Adults: 1 or 2 capsules or teaspoonfuls syrup three or four times daily. Children: 1 capsule or teaspoonful syrup three or four times daily. Infants: ½ teaspoonful syrup three or four times daily. (May be diluted with equal volume of water.) Bentyl 20 mg: Adults: 1 tablet three or four times daily. Bentyl Injection: Adults: 2 ml. (20 mg.) every four to six hours intramuscularly only. NOT FOR INTRAVENOUS USE. **MANAGEMENT OF OVERDOSE:** The signs and symptoms of overdose are headache, nausea, vomiting, blurred vision, dilated pupils, hot, dry skin, dizziness, dryness of the mouth, difficulty in swallowing, CNS stimulation. Treatment should consist of gastric lavage, emetics, and activated charcoal. Barbiturates may be used either orally or intramuscularly for sedation but they should not be used if Bentyl with Phenobarbital has been ingested. If indicated, parenteral cholinergic agents such as Urecholine<sup>®</sup> (bethanechol chloride USP) should be used.

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CARTA AL EDITOR

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November 1, 1979

Juan Aranda, MD  
Editor  
Boletín - P. R. Medical Association  
P. O. Box 9387  
Santurce, P. R. 00908

Dear Dr. Aranda:

Regretably there recently took place an inordinate amount of tasteless publicity both on television and the press concerning a gastric operation for obesity. It was to be a "first" in Puerto Rico. This publicity lasted for several weeks, so that it was next to impossible to reside in Puerto Rico and not know of this coming event that was to make medical history.

The unfortunate episode ended tragically with the death of the young woman, a death attributed to pulmonary embolization, and lacking the sobering benefit of an autopsy. Now Dr. Edward Mason, of the University of Iowa, originator of the operation and the man with probably the widest experience in its performance, in the August 1979 issue of the *Annals of Surgery*, states that early

post operative deaths are often attributed to pulmonary embolism, whereas the cause of death is more likely to have been peritonitis secondary to perforation. This has been documented through autopsy examination.

The above experience is unfortunate on many counts. First the tasteless publicity it received. Second the unfortunate outcome. Third, little was learned from the entire event. Last but not least it should serve to remind us that we cannot apply the experience of medical centers in the continental U. S. to our own medical reality, where certain of our hospitals may lack some of the more elaborate and advanced intensive care measures such as pulmonary artery and wedge pressures, etc.

Nevertheless what most distresses this writer in this case is the complete disregard of the most basic standards of medical ethics when dealing with press reports and television appearances. This to my mind is inexcusable and reprehensible.

Sincerely

José H. Amadeo, MD, FACS  
Chief, Surgical Service  
Veterans Administration Hospital  
San Juan, Puerto Rico

**MOVIMIENTO EN LA ESPINA LUMBAR DURANTE EJERCICIOS DE LAS EXTREMIDADES SUPERIORES. UN ESTUDIO RADIOLOGICO EN PACIENTES PARA — Y TETRAPLEGICOS.**

*Hein-Sorensen, O y Irstem, L. — Scand. J., Rehab. Med., 11: 13-27, 1979.*

Los ejercicios de fortalecimiento durante el tratamiento de pacientes con fracturas lumbares inestables producen un movimiento cifótico o lordótico sagital en la espina lumbar. Estos movimientos se han medido radiológicamente. Ejercicios de flexión de 45° en las articulaciones de los hombros causan un movimiento cifótico; mientras que la flexión a 110° y ejercicios de abducción a 90° producen un movimiento lordótico. La flexión de las caderas y rodillas a 45° producen un movimiento cifótico que se añade a los movimientos causados por los ejercicios de los hombros. El aumento en el peso de las extremidades superiores producen un aumento de todos los movimientos.

(Sometido por Rafael Seín, MD, VAH)

**EL GANGLIO ESFENOPALATINO: LOS EFECTOS REMOTOS INCLUYENDO SINTOMAS PSICOSOMATICOS, REACCIONES DE FURIA, DOLOR Y ESPASMOS**

*Ruskin, A. P.: Arch. Phys. Med. Rehabil., 60: 353: 359: August 1979.*

Muchos artículos que se han escrito implican al ganglio nasal en la producción de síntomas remotos

y discuten el tratamiento. Los síntomas son primordialmente espásticos, afectando tanto músculos viscerales y voluntarios incluyendo espasmos musculares del cuello, hombros y espalda; asma, hipertensión, espasmos intestinales; diarrea, angina de pecho, espasmos del utero ; hipo-incontrolado y otros. Todos estos síntomas aparentan tener 2 denominadores comunes, son mediados por el sistema nervioso autónomo y algunas veces pueden ser psicósomáticos. El ganglio esfenopalatino es un ganglio autónomo principal localizado superficialmente en la fosa pterigopalatina, con una distribución mayor, aferente a toda la nasofaringe y con conexiones con el nervio trigémino, facial, con el plexo simpático nervioso de la arteria carótida interna y como se demuestra en la rata, conexión directa con la pituitaria anterior.

Este artículo presenta argumentos que sostienen las siguientes hipótesis: (1) El ganglio esfenopalatino probablemente tiene una función crucial en los animales de baja especie, en disminuir las respuestas reflejas conocidas como reacciones de furia. (2) El ganglio, esfenopalatino es una puerta de entrada primordial al sistema autónomo expuesto a influencias patológicas y fácilmente accesible para intervenciones terapéuticas. (3) Una gran variedad de síntomas son producidos o mantenidos por una alteración en el tono del sistema autónomo y algunos de estos pueden ser afectados por la intervención al ganglio. (4) La posible relación entre algunos síntomas y condiciones psicósomáticas al sistema autónomo nervioso y la reacción de furia deben de ser considerados.

(Sometido por Rafael Seín, MD, VAH)



## DYSPHASIA ASSOCIATED WITH CRICOPHARYNGEAL DYSFUNCTION

Schultz, A., R., Niemtzw, P., Jacobs, S. R., Naso, F: *Arch. Phys. Med. Rehabil.* 60: 381: 386, 1979.

En los tipos de disfasia asociados con disfunción neuromuscular, miotonia del esfínter esofágico superior ha sido sugerida como tratamiento, sin embargo la literatura no está clara en cuanto a las indicaciones y resultados de este procedimiento. En este artículo se presentan 3 casos asociados con una falla en relajación del cricofaríngeo durante la deglución, 2 pacientes tenían infartos del tallo cerebral y el 3ro. una enfermedad inflamatoria del mismo. En todos los pacientes radiografiados con bario revelaron aspiración del material de contraste hacia la tráquea con falla en la relajación del esfínter cricofaríngeo. Las laringoscopias indirectas demostraron parálisis parcial de una o ambas cuerdas vocales. En un caso un EMG de los músculos laringeos, resultó normal. Una evaluación completa por el patólogo del habla no reveló anormalidades de la musculatura oral en ningún paciente. Todos los pacientes requirieron gastrostomías para sus necesidades nutricionales. Técnicas de alimentación terapéutica de parte del patólogo del habla incluyeron modificación y control de velocidad, cantidad consistencia del alimento junto con consejería para la prevención de aspiración. Alimentación oral sin aspiración fue lograda en 3 semanas por este método, lo que permitió el cierre de la gastrostomía. Por tanto la miotomía cricofaríngea no fue necesaria.

(Sometido por Jesús A. Maldonado, MD, VAH)

## RHEUMATOID ARTHRITIS, FAILURE OF DAILY HEAT THERAPY TO AFFECT ITS PROGRESSION

Mainardi, C. L., Waltur, J. M., Spiegel, P. K., Goldkamp, O. G., Harris, E. D., Jr.: *Arch. Phys. Med. Rehabil.* 60: 390-393, 1979.

Diecisiete voluntarios con artritis reumatoidea

simétrica fueron reclutados. Se les aplicó calor a una mano 2 veces por día por 2 años. La inflamación articular, dolor articular a la palpación y la fuerza del agarre fueron valorados a intervalos de tiempo. El aspecto proliferativo de la enfermedad fue evaluado por radiografías siguiendo un sistema de puntuación, no se encontró diferencia alguna entre la mano de control y la mano experimental en ninguno de los factores medidos. Los pacientes encontraron que la modalidad del calor los relajaba y los confortaba. Se llegó a la conclusión de que la terapia diaria con calor no acelera la lesión proliferativa de la artritis reumatoidea y puede seguirse usando como terapia conjunta en el tratamiento de esta entidad.

(Sometido por Jesús A. Maldonado, MD, VAH)

## ILIOLUMBAR SYNDROME AS A COMMON CAUSE OF LOW BACK PAIN: DIAGNOSIS AND PROGNOSIS

Hirschberg, G. G., Froetscher, L., Nacim, F.: *Arch. Phys. Med. and Rehab.*, September, 1979.

La mayoría de los casos de dolor de espalda caen en la categoría de dolor de espalda no específico en los cuales no se detecta ninguna patología por rayos X, exámenes de laboratorio o biopsias.

Las experiencias de los autores es que aproximadamente el 50 por ciento de los pacientes que caen en este grupo tienen un cuadro clínico que se caracteriza por signos y síntomas que se localizan en una cresta ilíaca. Los síntomas desaparecen temporalmente al infiltrarse la parte posterior de la cresta ilíaca correspondiente con lidocaína. Debido a la localización de los hallazgos y la etiología desconocida del síndrome, el término síndrome iliolumbar le es sugerido. Es importante distinguir el síndrome iliolumbar de las radiculitis, ya que esto evitaría muchas cirugías innecesarias. El síndrome iliolumbar crónico es una causa frecuente de incapacidad permanente de la espalda, algo que no se reconoce comunmente.

(Sometido por Tomás Poventud, MD, VAH)

## EDUCATIONAL AND TRAINING LEVELS AND EMPLOYMENT OF THE SPINAL CORD INJURED PATIENT

*El Ghatit, A. L., Hnason, R. W.: Arch. Phys. Med. Rehabil. 60: 405-406, 1976.*

En este artículo los autores proveen información sobre la educación y entrenamiento que siguen a una lesión traumática del cordón espinal. Ellos creen que este es un renglón importante de estudio, ya que la educación y entrenamiento (1) provee a individuos con una incapacidad física una forma constructiva y significativa de utilizar su tiempo, (2) contribuye a que el paciente se sienta útil, (3) aumenta la probabilidad de interacción social, ya que el individuo se relaciona con otras personas con metas similares, y (4) aumenta la posibilidad de obtener un empleo productivo.

Se hicieron cuestionarios de seguimiento a 745 veteranos con lesión al cordón espinal, 40 por ciento reportaron que ellos habían mejorado su educación después de su incapacidad; la educación post-daño no se relaciona al nivel del daño. Una relación significativa se encontró entre el estado marital y un mejor aprovechamiento en los estudios en pacientes solteros, separados o divorciados; un matrimonio exitoso se asocia a mejor aprovechamiento en la educación. Los que tenían un "status" educacional alto o que mejoraron su educación después del daño tenían más posibilidad de conseguir empleo.

(Sometido por Verónica Rodríguez, MD, VAH)

## EXTENSION OF MYOCARDIAL INFARCTION: INCIDENCE AND PROGNOSIS

*Fraker, T., Wagner, G., Rosati, R.: Circulation 60: 1126, 1979.*

En este estudio se analizan 58 episodios de extensión de infarto de miocardio agudo. La incidencia de extensión de infarto fue 13 por ciento (58/458).

Los pacientes con extensión tuvieron una mortalidad hospitalaria de 36 por ciento comparado con 9 por ciento en los pacientes sin extensión. La supervivencia a un año de seguimiento luego de dados de alta fue de 76 por ciento en los pacientes con extensión de infarto y 91 por ciento en los pacientes sin extensión.

Los autores sugieren intervenciones terapéuticas más tempranas y más agresivas en los pacientes con extensión de infarto para tratar de disminuir esta mortalidad alta.

(Sometido por G. Cintrón, MD, VAH)

## THE EFFECT OF ORTHOTIC TREATMENT OF SPINA BIFIDA PATIENTS

*Sankarankutty-Spina Bifida Therapy, 1:4:187-196, 1979.*

Un análisis del status ambulatorio de 102 pacientes con meningocele encontró que del 51 por ciento que tenía lesión dorsal baja neurológica, 5.7 por ciento podían caminar en sus comunidades y solo 1.75 por ciento estaban sujetos a sillas de rueda, mientras que el resto eran ambuladores no funcionales y ambuladores dentro de la casa (con aparatos). Del 41.2 por ciento con lesiones lumbares, 45.2 por ciento podían caminar en la comunidad, 21.4 por ciento estaban limitados al hogar, 31 por ciento eran andadores no funcionales y 2.4 por ciento de silla de rueda, eran dependientes. Ocho pacientes en el estudio tenían lesiones sacrales, 7 podían caminar en la comunidad y uno estaba limitado a la casa. Se concluye que aunque varios factores determinan la habilidad del paciente con mielomeningocele para caminar, este estudio sugiere que un "approach" ortótico quirúrgico es vital.


(Sometido por Rafael Alvarez, MD, VAH)

# Breast self-examination: KEY ROLE OF THE PHYSICIAN

<b>item:</b>	Breast cancer is a major concern of American women, according to a recent Gallup study conducted for the American Cancer Society.
<b>item:</b>	Although aware that early discovery improves the chances of cure, and that BSE can lead to early discovery, <i>fewer than 1 in 5</i> women practice BSE, and <i>only half</i> have an annual breast examination by a physician.
<b>item:</b>	Only 35% of all women polled reported that a <i>physician</i> had ever raised the subject of breast self-examination, and only 24% had received instruction from the physician on how to do it. Even among women who regularly see a gynecologist, only 34% had been instructed on BSE.
<b>item:</b>	<i>But</i> , among women who received personal instruction from their physicians, the overwhelming majority (92%) practiced BSE during the preceding year.

The Gallup study revealed that, far more important than increasing awareness of breast self-examination, is the problem of inducing women to practice it regularly. The physician plays a key role in this—by teaching women the correct technique, and instilling in them the confidence that will assure their continued practice of BSE. The American Cancer Society gives

major emphasis to breast cancer through research and a vast array of public educational materials, designed to give women life-saving information about the disease. Our latest approach is via a pioneering television film starring Jennifer O'Neill, "Breast Cancer: Where We Are." Where we *will* be in a few years will certainly hinge on our joint efforts.

**American Cancer Society** 



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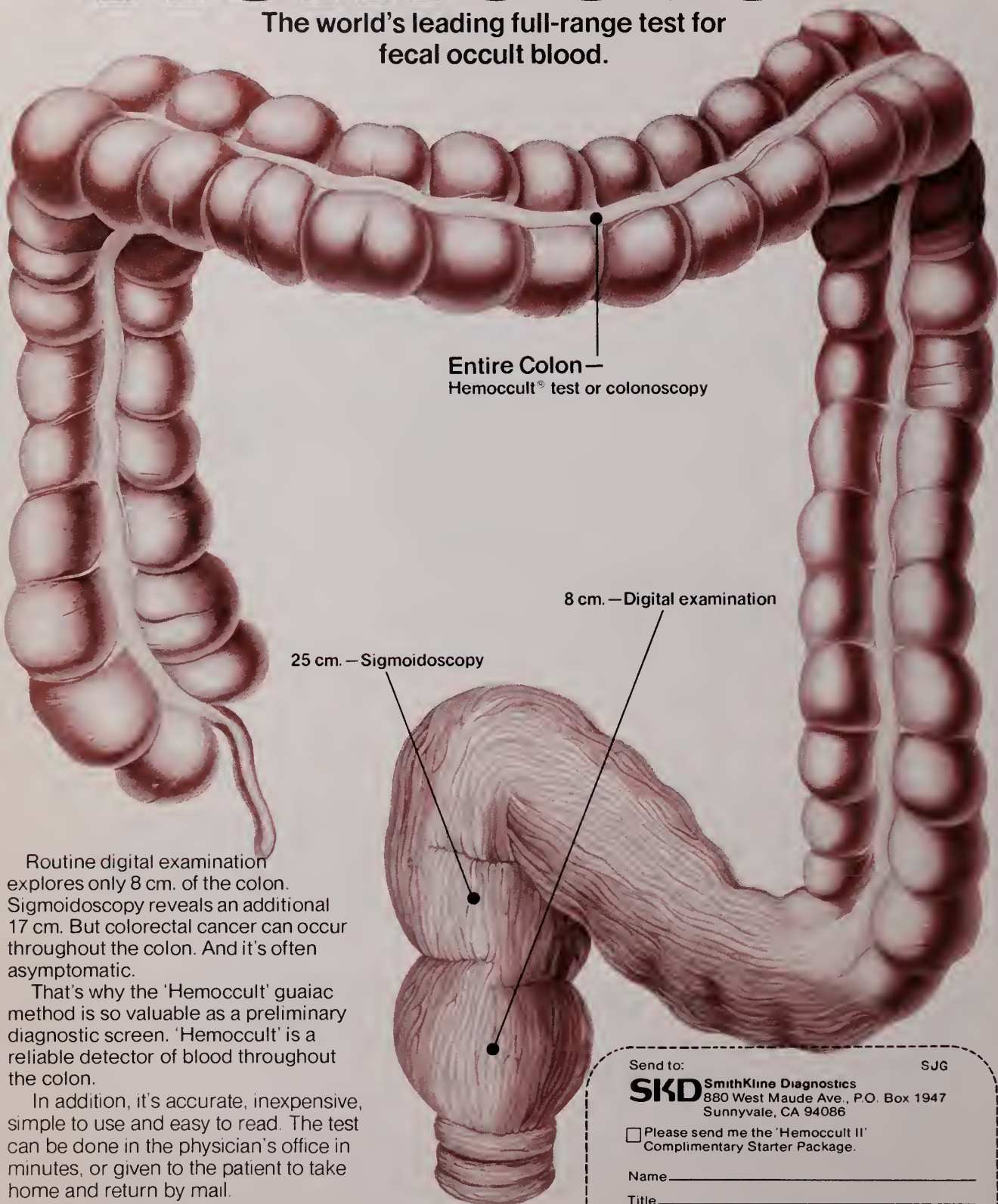
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## OPPORTUNISTIC LUNG INFECTION DUE TO "PITTSBURG PNEUMONIA AGENT"

Myerowitz, et al: *New Eng. J. Med.* 301: 953-958, 1979

## OPPORTUNISTIC PNEUMONIA: A CLINICOPATHOLOGICAL STUDY OF FIVE CASES CAUSED BY AN UNIDENTIFIED ACID FAST BACTERIUM

B..H. Rogers, et al: *New Eng. J. Med.* 301: 959-961, 1979.

## ANOTHER NEW PNEUMONIA: PANDORA'S BOX REOPENED

Editorial. Morton N. Schwartz. *New Eng. J. Med.* 301: 995-996, 1979.

En los artículos arriba mencionados se describe una nueva etiología para pulmonías en el paciente inmunocomprometido. Este nuevo agente es ácido resistente, no crece en medios de cultivos comunes, es gram-negativo y se cultiva en huevos embrionados y en coballos. Este nuevo agente es diferente al agente de la enfermedad de los legionarios o *Legionella pneumophila*. Esta pulmonía ocurre en pacientes inmunocomprometidos que han recibido corticoesteroides recientemente. Se manifiesta por un cuadro neumónico no específico y patológicamente los alveolos están llenos de células inflamatorias y hay pleuritis severa. Es una enfermedad seria con mortalidad alta. Se requiere tejido pulmonar para hacer el diagnóstico, por lo tanto un paciente inmunocomprometido con un infiltrado pulmonar en donde se desconoce la etiología requiere una biopsia.

Este nuevo microorganismo, es susceptible *in vitro* a sulfa-trimetropin, rifampin y eritromicina. No hay evidencia de efectividad *in vitro*. Debemos de estar alertas de esta nueva condición para sospecharla y poder diagnosticarla.

(Sometido por Carlos H. Ramírez Ronda, MD)

## THE EFFECT OF AN EXERCISE PROGRAM ON CHANGE IN CURVE IN ADOLESCENTS WITH MINIMAL IDIOPATHIC SCOLIOSIS

Stone B., *Phys. Therapy*, 59: 6: 759-763, June, 1979.

Después de participar en un programa de ejercicios entre 9 a 15 meses, 42 adolescentes con escoliosis mínima idiopática, fueron evaluados para determinar la influencia del programa en el cambio de sus curvaturas. Considerando una diferencia de 4 grados o más entre medida inicial y final de la curva como cambio significativo, 5 por ciento de las curvas aumentaron, 74 por ciento permanecieron iguales y 21 por ciento disminuyeron. Cambio en curvatura para estos pacientes fue comparada con aquella de un grupo correspondiente seleccionado de adolescentes con escoliosis que no había participado en el programa de ejercicios. No se encontró diferencia significativa en el cambio de curva entre los 2 grupos. Para los pacientes que habían practicado los ejercicios, no había relación significativa entre cambio en curva y extensión de actividad física, ni entre cambio en curva y habilidad para recordar ejercicios; actuación correcta, o frecuencia de actuación. Se discute posibles explicaciones para los resultados del estudio y se discuten las limitaciones de su diseño. Data tabular incluida.

(Sometido por Rafael Alvarez, MD, VAH)

## NEONATAL SPINAL CORD INJURY

Koch, B.. M., Eng, G. M.: *Arch. Phys. Med, Rehabil.* 60: 378-381, 1979.

La primera descripción de Trauma al Cordón Espinal del Neonato fue hecha en 1869. Los autores estudiaron 14 casos, tres de los cuales fueron pacientes

recientes y diez en revisión de la literatura. Todos se caracterizaron por ser partos difíciles, doce de los cuales fueron presentación "breech". Las lesiones al cordón espinal variaron desde C1-C2 hasta T-12. Ocho murieron: de seis que sobrevivieron, cinco tienen una edad mental normal según exámenes de inteligencia.

El mecanismo de trauma depende del método de extracción, en su mayoría hubo presentación "breech" e hiperextensión de la cabeza. La tracción sobre las piernas con la cabeza relativamente fija por contracción uterina puede promover ruptura espinal. En el examen físico los bebés tienen varios grados de dificultad para el comienzo de la respiración espontánea y varios diferentes signos de daño neurológico dependiendo del nivel y grado de la lesión. Problemas respiratorios, urinarios y de disfunción neurológica, incluyendo el Sistema Autónomo, son comunes.

El diagnóstico diferencial incluye enfermedad de Werdnig-Hoffmann, meningomielocoele, mielitis transversa, tumores del cordón espinal, hipotemia cerebral y otros.

El pronóstico de cada caso se puede determinar por examen neurológico y el uso de electromiografía para determinar con certeza el nivel de la lesión y el grado de esta. Infantes con lesiones que les permiten vivir aunque con espasticidad, paraplejia y problemas de control de esfínteres serán los de mayor preocupación para el equipo médico. Estos pacientes tendrán iguales problemas que otros pacientes parapléjicos y de trauma al cordón espinal con el factor adicional de que son niños en etapas de crecimiento, creando un reto especial por los problemas propios que su desarrollo y adaptación presenta.

(Sometido por Frank W. López, MD, VAH)

## ESTABLISHING ACTIVITY AND TRAINING LEVELS FOR PATIENTS WITH ISCHEMIC HEART DISEASE

*Amundsen, L.: Physical Therapy: 59:754-758, 1979.*

Se ha demostrado que los pacientes con enfer-

medad isquémica del corazón se benefician con el establecimiento de un programa de entrenamiento y actividades físicas adecuado a su condición. Se puede determinar el gasto de energía y pulso apropiado a cada paciente usando un examen de tolerancia de ejercicio (graded, Exercise Tolerance Test).

El grupo del autor comienza por incluir un resumen del historial médico del paciente sobre la condición cardíaca e incluye la consideración de otras condiciones médica y limitaciones físicas del sujeto. Esto se complementa con un examen físico en que se determina la condición del paciente en su totalidad, dirigido hacia las posibilidades de éste para ejercitarse. Por último se complementa con el examen de tolerancia de ejercicios. A modo de conseguir una aceptación mayor por parte del enfermo, se toma en cuenta las preferencias recreativas, deportivas, actividades de trabajo, etc., del individuo, en la selección del programa de actividades a seguir. El nivel de intensidad de los ejercicios a seguir se determinan a base de los milímetros de  $O_2$  por kilogramo de peso por minuto o en METs (equivalente metabólico). Con esta medida a su vez se determina la intensidad de actividades ocupacionales y las pulsaciones cardíacas apropiadas en el programa a establecerse.

El éxito del establecimiento de un programa de rehabilitación para pacientes con enfermedad isquémica del corazón requiere de los conocimientos de los patrones antes mencionados y la disponibilidad del equipo adecuado para determinar las capacidades del paciente.

Incluye tablas e ilustraciones sobre los parámetros y ejercicios discutidos.

(Sometido por Frank W. López, MD, VAH)

## STREPTOCOCCUS BOVIS SEPTICEMIA AND CARCINOMA OF THE COLON

*Annals of Internal Medicine 1979; 91: 560-562*

Se evaluaron prospectivamente pacientes con septicemia por *Streptococcus bovis* buscando lesiones gastrointestinales. Este estudio se llevó a cabo por el hallazgo de estudios previos asociados con el recobro

de este organismo en pacientes con carcinoma del colon. Se estudiaron 29 pacientes con 30 episodios de septicemia por *S. bovis*. Se hicieron evaluaciones completas en 15 pacientes que incluyeron colonoscopia, cirugía o examen por autopsia. En 8 pacientes se encontró carcinoma del colon, y en dos se encontró carcinoma del esófago. De los catorce pacientes en que no se pudo completar una evaluación gastrointestinal adecuada se encontró uno con carcinoma del estómago, uno con linfoma gástrico y tres con masas del colon que no se obtuvo diagnóstico final. Diecinueve (19) pacientes no tuvieron signos gastrointestinales ni síntomas y sus excretas no tuvieron sangre oculta al admitirse al hospital. Todo paciente que se le diagnostica septicemia por *S. bovis* necesita una evaluación completa del tracto gastrointestinal, especialmente del colon.

(Sometido por Ramón H. Bermúdez, MD)

#### CLINICAL INDICATORS OF LEFT MAIN CORONARY ARTERY DISEASE IN UNSTABLE ANGINA

The value of clinical and non-invasive data in

assessing left main coronary artery disease (LMCAD) in patients with unstable angina was evaluated using two hundred consecutive catheterized patients. They were sub-divided into two groups: those with 50 percent or greater narrowing (subgroup A: 750 percent  $< 70$  percent; subgroup B:  $> 70$  percent) and those with less than 50 percent narrowing of LMCA. Only 35 patients (17.5 percent) had LMCAD of whom 10 had 50 to 70 percent narrowing and 25 had  $\geq 70$  percent narrowing. The rest 165 patients had minimal to no narrowing. No significant differences in age, sex, history of previous myocardial infarction, C.H.F., duration of longest episode of pain nor the presence of dyspnea with pain was found between both groups. Triple-vessels coronary involvement and collaterals were more common in group I patients. Transient ST-segment depression and T-wave changes were more common than transient ST-segment elevation. Crescendo angina, transient ST-segment depression with pain, simultaneous ST segment shifts in anterior and inferior leads and fluoroscopic calcification near the left main were more common in patients with LMCAD, however coronary arteriography remains as the most reliable test to assess the presence of significant obstruction of the trunk of the left coronary artery.

(Submitted by José Conto, MD, VAH)



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Exhortamos a los patronos (y otros contribuyentes) que tengan facilidades de computadoras a usar el medio magnético para rendir la Forma 499R-2/W-2PR. Los patronos que ya usan este medio han encontrado que es eficiente, flexible y ahorra dinero. Usted puede obtener las especificaciones para rendir en medio magnético escribiendo a: Social Security Administration, Bureau of Data Processing, P. O. Box 2317, Baltimore, Maryland 21203.

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Effective January 1, 1979 all employers in Puerto Rico will begin to use only one form to report the income tax withheld to the Department of the Treasury of Puerto Rico and the social security tax withheld to the Social Security Administration.

To this effect, a new form has been jointly designed by the Department of the Treasury of Puerto Rico, the U. S. Internal Revenue Service, and the Social Security Administration. This form will combine the Forms 499R-2 used by the Commonwealth of Puerto Rico and Forms W-2 used by the Federal Government.

Under this new system, the employer will fill out one 499R-2/W-2PR for each employee and will distribute it as follows:

1. Original to the Social Security Administration.
2. Copy A to the P. R. Income Tax Bureau.
3. Copy B for the employee's income tax return.
4. Copy C for the employee's records.
5. Copy D for the employer's records.

The original copy of the Forms 499R-2/W-2PR should be filed with the Social Security Administration no later than the last day of February of the year following the year for which taxes are withheld. The original copy will be accompanied by Form W-3PR which will be furnished to the employer by the U. S. Internal Revenue Service. Mail these forms to the following address:

Social Security Administration  
B. D. P.  
Baltimore, Maryland 21290

Copy A should be filed with the Department of the Treasury of Puerto Rico no later than January 31 of the year following the year of retention. Copy A will be accompanied by Form 499R-3 PR (Reconciliation Statement) which will be furnished by the Department of the Treasury of Puerto Rico. Mail these forms to the following address:

Bureau of Income Tax  
Employer's Section-Office 608  
Box S-2501  
San Juan, Puerto Rico 00903

Forms 941PR, 942PR, and 943PR no longer include schedule A which listed the quarterly earnings of each employee.

We encourage employers (and other tax payers) with computer capability to use magnetic media for filing Form 499R-2/W-2PR. Employers that have used this method find that reporting on magnetic media saves money, is efficient and flexible. You can get the specifications for reporting Form 499R-2/W-2PR information on magnetic media by writing to: Social

Security Administration, Bureau of Data Processing, P. O. Box 2317, Baltimore, Maryland 21203.

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#### AMA NEWS:

#### X-RAY SCREENING VALUABLE IN FINDING BREAST CANCER

Chicago — Value of early discovery of breast cancer and consequent successful treatment far outweighs any slight possible health hazard from X-ray screening of women's breasts, say two separate reports in the Nov. 9 Journal of the American Medical Association.

Mammography, X-raying of the breasts, is now carried out at very low doses of exposure, Dr. Stephen A. Feig, Philadelphia radiologist, points out. Formerly the exposure was 7 to 15 rads. Now exposure is reduced to 0.5 to 9.9 rads.

Low-dose systems are a relatively new innovation. They are now used for the majority of mammographic examinations in the United States, Dr. Feig says.

"Although the hypothetical risk from low doses of medical radiation is immeasurably small, these figures indicate that mammography can be undertaken with much less cause for concern than before," he declares. The risk is so small that low-dose mammographic examination of one million women might result in one excess breast cancer per year after a ten-year latent period, he says.

This may be compared with a breast cancer incidence of from 1,000 to 2,000 cases per one million women per year. Half of these cases might be detected by mammography at an early stage, he says.

Dr. Feig lists the guidelines for mammographic examinations of the American College of Radiology. Women with breast lumps or other physical findings should be X-rayed promptly. In screening of women with no symptoms, an X-ray between the ages of 35 and 40 years is recommended. Subsequent X-rays should then be performed at one to three-year intervals, unless other symptoms appear. After age 50 years, annual or other regular interval X-rays should be taken.

In another report in the same issue of the Journal, a research team from the University of Arizona, Tucson, reports on a study of sensitivity of mammography and physical examination of the breast for detecting breast cancer.

Mammography detected 62 percent of the small, early cancers, while physical examination — feeling the breast for lumps — found only 24 per cent. The two techniques together detected 75 per cent of the cancers. Most of the cancers were very small — one centimeter or less — on discovery, and were susceptible to successful treatment.

#### NEW METHODS IDENTIFY RISK OF BIRTH DEFECTS AMONG BABIES BORN TO OLDER MOTHERS

Chicago — Medical science has long been aware that birth defects occur more frequently among infants born to older women.

However, it is now possible to determine early in pregnancy if the infant is likely to suffer severe abnormalities, says a report in the November 13 Journal of the American Medical Association. Thus older women who choose to become pregnant can take advantage of recent advances in diagnosis that offer an opportunity to identify the risk of bearing a child with disorders or defects and consider elective abortion.

In an Atlanta, Ga. study, doctors found that, with the new techniques, women aged 35 to 44 years have no greater risk of bearing an infant with a detectable severe birth defect than do younger women.

The report is by Marshall F. Goldberg, MD, of the Center for Disease Control in Atlanta.

In an accompanying editorial, Norman Fost, MD, of the University of Wisconsin, Madison, points out that the new diagnostic techniques will by no means find all potential birth defects, but they can reduce the risk of bearing an affected infant.

Dr. Fost contends that prenatal diagnosis is ultimately a birth-facilitating rather than a birth-preventing service. More than 95 per cent of the diagnoses in the womb disclose no abnormality of the fetus.

“For the older woman,” says Dr. Fost, “the availability of such services makes conception acceptable where previously it was often avoided because of irrational fears or the rational desire to avoid even a small risk of having an affected child.”

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#### AMA PUBLISHES GUIDELINES FOR EXAMINING PILOTS

Chicago — A document for the guidance of physicians in examining airplane pilots with possible nervous system disease or injuries will be published this month by the American Medical Association.

The 225-page report, prepared by the AMA for the Federal Aviation Administration, will be published as a special supplement to the November issue of the AMA's specialty journal, Archives of Neurology. The book was prepared by the AMA in collaboration with experts of the American Academy of Neurology and the American Association of Neurological Surgeons.

The guidelines are not official policy for the AMA, American Academy of Neurology or American Association of Neurological Surgeons, but are intended only to serve as aids to physicians in examining pilots. The examining doctor neither issues nor denies license. Authority to issue or deny civil medical certifications to pilots rests with the FAA.

“In 1976 there were 744,246 persons in the U. S. with airmen's certificates, of which 45,072 were for air transports and 187,801 were for commercial flying,” points out Theodore C. Doege, M. D., AMA Director of Environmental, Public and Occupational Health and project director for the document.

Many American physicians are actively involved in aviation medicine, Dr. Doege says. They examine airline pilots twice yearly and commercial pilots once yearly. In 1976 these physicians sent to the FAA reports on more than 450,000 medical examinations.

“We of AMA believe this study will be valuable in future years as a benchmark to be used by the FAA, and by tens of thousands of the nation's physicians. It will contribute not only to the health of the nation's



pilots, but also to the safety and welfare of millions of its other citizens."

Specialists in various aspects of the brain and its problems developed eight chapters in the book, dealing with stroke, brain tumors, head injuries, diseases such as multiple sclerosis, neuromuscular disorders, epilepsy, severe headache and dizziness. Each is examined to determine at what point the individual pilot is no longer safe in the cockpit.

Throughout, the emphasis is on helping pilots to keep flying rather than merely grounding everyone with a physical problem. An individual with a history of a succession of small strokes, however, would be ruled out from flying, for he or she might have another stroke in the air. A history of brain tumor does not in itself disqualify a pilot. It is his or her present condition that should be evaluated. Pilots who have sustained moderate or severe head injury should be required to undergo simulator or flight testing before being returned to flight status.

Men and women who suffer from migraine headache in adolescence and early adult life are poor risks for aviation, the guide declares. Under the stress of flying, the migraine tendency is likely to become more of a problem. The patient with classic migraine is always at high risk and should not be a pilot or member of a crew.

The special supplement will be distributed to the more than 16,000 subscribers of *Archives of Neurology*. Additional copies are available from Order Department, OP-30, American Medical Association, P. O. Box 821, Monroe, WI 53566. Cost is \$3.00 per copy.

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#### AMA SCHEDULES CONFERENCE ON SPORTS MEDICINE

Chicago — The 21st American Medical Association Conference on the Medical Aspects of Sports will be held next Jan. 12 at San Antonio.

"Sports Medicine for the Primary Care Physician" will be the theme of the conference.

Sports medicine experts from across the nation

will discuss such topics as women in sports, the physical exam for the young athlete, heart evaluation of the young athlete, elbow injuries in young ball players, knee injuries, back injuries, injuries to the hand, the role of radiology and nuclear medicine in evaluating athletic injuries, prevention of injuries and violence in sports.

Keynote luncheon speaker for the conference will be Kenneth H. Cooper, MD, executive director of the Aerobics Center, The Cooper Clinic, Dallas. Dr. Cooper is a national authority on exercise and physical conditioning.

Use of regular daily exercise is being extensively studied as a means of reducing or delaying the onset of heart disease, Dr. Cooper has declared. Other systems of the body also gain from regular exercise. But an exercise program should be properly implemented for a safe start. Dr. Cooper's latest book, "The Aerobic Way," presents new data gained from his work at the Aerobics Center in Dallas.

Dr. Donald Cooper, of Stillwater, Okla., emphasized that we are seeing less and less of pre-participation physical examinations today. Laws such as the requirement that women be given equal emphasis in school sports have brought participation in sports by some for which it is dangerous, he says.

Prevention of injuries in football, says Dr. Joe Torg of Philadelphia, depends greatly on the philosophy of the coach. The older, more mature coach who sees the game as part of the educational experience, to be played as a contest of skill, strategy, team work and discipline will have few injuries, Dr. Torg says.

Other program participants will include Leatha Y. Hunter, MD, orthopedic surgeon, University of Michigan, Ann Arbor; William B. Strong, MD, pediatric cardiologist, Medical College of Georgia, Augusta; Kay E. Wilkins, MD, orthopedic surgeon, University of Texas Medical School, San Antonio.

Bernard R. Cahill, MD, orthopedic surgeon, Peoria, Ill.; Arvo Neidre, MD, orthopedist, University of Texas Medical School, San Antonio; Jerry D. Julian, MD, orthopedic surgeon for the athletic department of the University of Texas, Austin; Frank C. McCue, MD, orthopedist and rehabilitation specialist, University of Virginia Medical Center, Charlottesville, Va.; Jack W. Bowerman, MD, radiologist, of Johns Hopkins School of Medicine, Baltimore; S. Harvard Kaufman, MD, psychiatrist, Seattle, Wash.

Further information on the conference is available from the Department of Environment, Public and Occupational Health, American Medical Association, 535 N. Dearborn St., Chicago, IL 60610.

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#### *FROM THE AMERICAN COLLEGE OF SPORTS MEDICINE*

#### *AMERICAN COLLEGE OF SPORTS MEDICINE OPINION STATEMENT ON THE PARTICIPATION OF THE FEMALE ATHLETE IN LONG-DISTANCE RUNNING*

In the Olympic Games and other International contests, female athletes run distances ranging from 100 meters to 3,000 meters, whereas male athletes run distances ranging from 100 meters through 10,000 meters as well as the marathon (42.2 km). The limitation on distance for women's running events has been defended at times on the grounds that long-distance running may be harmful to the health of girls and women.

#### *Opinion Statement*

It is the opinion of the American College of Sports Medicine that females should not be denied the opportunity to compete in long-distance running. There exists no conclusive scientific or medical evidence that long-distance running is contraindicated for the health, trained female athlete. The American College of Sports Medicine recommends that females be allowed to compete at the national and international level in the same distances in which their male counterparts compete.

#### *Supportive Information*

Studies (10, 32, 41) have shown that females respond in much the same manner as males to systematic exercise training. Cardiorespiratory function is improved as indicated by significant increases in maximal oxygen uptake (4, 6, 13, 16, 30). At maximal

exercise, stroke volume and cardiac output are increased after training (30). At standardized submaximal exercise intensities after training, cardiac output remains unchanged, heart rate decreases, and stroke volume increases (6, 30, 31). Also, resting heart rate decreases after training (30). As is the case for males, relative body fat content is reduced consequent to systematic endurance training (33, 35, 51).

Long-distance running imposes a significant thermal stress on the participant. Some differences do exist between males and females with regard to thermoregulation during prolonged exercise. However, the differences in thermal stress response are more quantitative than qualitative in nature (36, 38, 47). For example, women experience lower evaporative heat losses than do men exposed to the same thermal stress (29, 40, 53) and usually have higher skin temperatures and deep body temperatures upon onset of sweating (3, 18, 45). This may actually be an advantage in reducing body water loss so long as thermal equilibrium can be maintained. In view of current findings (10, 11, 15, 40), it appears that the earlier studies which indicated that women were less tolerant to exercise in the heat than men (36, 53) were misleading because they failed to consider the women's relatively low level of cardiorespiratory fitness and heat acclimatization. Apparently, cardiorespiratory fitness as measured by maximum oxygen uptake is a most important functional capacity as regards a person's ability to respond adequately to thermal stress (9, 11, 15, 57). In fact, there has been considerable interest in the seeming cross-adaptation of a life style characterized by physical activity involving regular and prolonged periods of exercise hyperthermia and response to high environmental temperatures (1, 37, 39). Women trained in long-distance running have been reported to be more tolerant of heat stress than non-athletic women matched for age and body surface area (15). Thus, it appears that trained female long-distance runners have the capacity to deal with the thermal stress of prolonged exercise as well as the moderate-to-high environmental temperatures and relative humidities that often accompany these events.

The participation of males and females in road races of various distances has increased tremendously during the last decade. This type of competition attracts the entire spectrum of runners with respect to ability—from the elite to the novice. A common fea-

ture of virtually all of these races is that a small number of participants develop medical problems (primarily heat injuries) which frequently require hospitalization. One of the first documentations of the medical problems associated with mass participation in this form of athletic competition was by Sutton and co-workers (46). Twenty-nine of 2,005 entrants in the 1971 Sidney City-to-Surf race collapsed; seven required hospitalization. All of the entrants who collapsed were males, although only 4 percent of the race entrants were females. By 1978 the number of entrants increased approximately 10 fold with females accounting for approximately 30 percent of the entrants. In the 1978 race only nine entrants were treated for heat injury and again all were males (43). In a 1978 Canadian road race, in which 1,250 people participated, 15 entrants developed heat injuries—three females and 12 males, representing 1.3 percent and 1.2 percent of the total number of female and male entrants, respectively (27). Thus, females seem to tolerate the physiological stress of road race competition at least as well as males.

Because long-distance running competition sometimes occurs at moderate altitudes, the female's response to an environment where the partial pressure of oxygen is reduced (hypoxia) should be considered. Buskirk (5) noted that, although there is little information about the physiological responses of women to altitude, the proportional reduction in performance at Mexico City during the Pan American and Olympic Games was the same for males and females. Drinkwater et al. (13) found that women mountaineers exposed to hypoxia demonstrated a similar decrement in maximal oxygen uptake as that predicted for men. Hannon et al. (23, 24) have found that females tolerate the effects of altitude better than males because there appears to be both a lower frequency and shorter duration of mountain sickness in women. Furthermore, at altitude women experience less alterations in resting heart rate, body weight, blood volume, electrocardiograms, and blood chemistries than men (23, 24). Although one study has reported that women and men experience approximately the same respiratory changes with altitude exposure (44), another (22) reports that women hyperventilate more than men, thereby increasing the partial pressure of arterial oxygen and decreasing the partial pressure of arterial carbon dioxide. Thus, females tolerate the stress of altitude at least as well as men.

Long-distance running is occasionally associated with various overuse syndromes such as stress fracture, chondromalacia, shinsplints, and tendonitis. Pollock et al. (42) have shown that the incidence of these injuries for males engaged in a program of jogging was as high as 54 percent and was related to the frequency, duration, and intensity of the exercise training. Franklin et al (19) recently reported the injury incidence of 42 sedentary females exposed to a 12-week jogging program. The injury rate for the females appeared to be comparable to that found for males in other studies although, as the investigators indicated a decisive interpretation of presently available information may be premature because of the limited orthopedic injury data available for women. It has been suggested that the anatomical differences between men's and women's pelvic width and joint laxity may lead to a higher incidence of injuries for women who run (26). There are no data available, however, to support this suggestion. Whether or not the higher intensity training program of competitive male and female long-distance runners result in a difference in injury rate between the sexes is not known at this time. It is believed, however, that the incidence of injury due to running is related more to distances run in training, the running surfaces encountered, biomechanics of the back, leg and foot, and to foot apparel (28).

Of particular concern to female competitors and to the American College of Sports Medicine is evidence which indicates that approximately one-third of the competitive female long-distance runners between the ages of 12 and 45 experience amenorrhea or oligomenorrhea for at least brief periods (7, 8). This phenomenon appears more frequently in those women with late onset of menarche, who have not experienced pregnancy, or who have taken contraceptive hormones. This same phenomenon also occurs in some competing gymnasts, swimmers, and professional ballerinas as well as sedentary individuals who have experienced some instances of undue stress or severe psychological trauma (25). Apparently, amenorrhea and oligomenorrhea may be caused by many factors characterized by loss of body weight (7, 21, 25). Running long distances may lead to decreased serum levels of pituitary gonadotrophic hormones in some women and may directly or indirectly lead to amenorrhea or oligomenorrhea. The role of running and the pathogenesis of these menstrual irregularities



remains unknown (7, 8).

The long-term effects of these types of menstrual irregularities for young girls that have undergone strenuous exercise training are unknown at this time. Eriksson and co-workers (17) have reported, however, that a group of 28 young girl swimmers, who underwent strenuous swim training for 2.5 years, were normal in all respects, (e. g., childbearing) 10 years after discontinuing training.

In summary, a review of the literature demonstrates that males and females adapt to exercise training in a similar manner. Female distance runners are characterized by having large maximal oxygen uptakes and low relative body fat content. The challenges of the heat stress of long-distance running or the low partial pressure of oxygen at altitude seem to be well tolerated by females. The limited data available suggest that females, compared to males, have about the same incidence of orthopedic injuries consequent to endurance training. Disruption of the menstrual cycle is a common problem for female athletes. While it is important to recognize this problem and discover its etiology, no evi-

dence exists to indicate that this is harmful to the female reproductive system.

(Supporting references available on request from the American College of Sports Medicine, 1440 Monroe Street, Madison, Wisconsin 53706.)

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Héctor F. Rodríguez-Estape, MD, Ponce, Puerto Rico, American College of Cardiology Governor for the Commonwealth of Puerto Rico, announced that the following cardiovascular specialists in his geographic area have achieved the ACC's membership rank of Fellowship:

Mario B. Muñoz Torres, MD, Ponce, Puerto Rico.  
Juan M. Aranda, MD, San Juan, Puerto Rico.

## M E D I Q U I Z

1. En la evaluación de un paciente nuevo con evidencia de insuficiencia mitral significativa, la presencia de ritmo sinusal y un atrio izquierdo normal sugieren:
  - a. insuficiencia mitral crónica
  - b. insuficiencia mitral aguda
2. En un paciente adulto mayor de 40 años, la presencia de dolor precordial sugiere:
  - a. enfermedad coronaria
  - b. hipertensión pulmonar
  - c. A y B
  - d. ninguna
3. La arritmia mas significativa asociada con el síndrome de Wolff-Parkinson-White es fibrilación o aleteo atrial paroxístico con respuesta ventricular rápida.

CIERTO o FALSO

4. Digital es la droga de elección en el tratamiento de fibrilación o aleteo atrial paroxístico asociado con el síndrome de Wolff Parkinson-White.

CIERTO o FALSO

5. La presencia de un tracto atrio-ventricular accesorio siempre se puede diagnosticar con trazados electrocardiográficos seriados.

CIERTO o FALSO

6. La característica más importante para diagnosticar angina variante es:
  - a. dolor precordial nocturno
  - b. mejoría clínica con nitroglicerina
  - c. Elevación transitoria del segmento ST durante el dolor
  - d. prematuros ventriculares durante el dolor de pecho

7. Todos estos agentes anti-arítmicos pueden terminar la taquicardia por reentrada atrio-ventricular, aumentando el período refractario del nodo atrio-ventricular excepto:
- a. propranolol
  - b. Verapamil
  - c. degoxin
  - d. quinidina
8. En el músculo cardíaco todos excepto uno de los siguientes factores son determinantes del consumo de oxígeno por el miocardio:
- a. frecuencia cardíaca
  - b. presión sistólica
  - c. contractilidad cardíaca
  - d. flujo coronario
  - e. tensión intramiocárdica
9. El estudio completo de la actividad eléctrica del haz de His y estructuras adyacentes no requiere estimulación eléctrica del corazón

CIERTO o FALSO

10. En cuál de las siguientes condiciones estaría usted menos inclinado a recomendar la implantación de un marcapaso:
- a. Bloqueo atrio-ventricular de segundo grado (Mobitz Tipo II)
  - b. Síndrome de Bradicardia-Taquicardia
  - c. Bradicardia sinusal con prematuros ventriculares frecuentes y tardes en el ciclo cardíaco.
  - d. Bradicardia sinusal con latidos de escape en la unión atrio-ventricular.
  - e. Bradicardia sinusal con fallo congestivo cardíaco.

(Contestaciones en página 433)



## Instrucciones para los Autores

El Boletín acepta para su publicación artículos relativos a medicina y cirugía y las ciencias afines. Igualmente acepta artículos especiales y correspondencia que pudiera ser de interés general para la profesión médica.

El artículo, si se aceptara, será con la condición de que se publicará únicamente en esta revista.

Para facilitar la labor de revisión de la Junta Editora y la del impresor, se requiere de los autores que sigan las siguientes instrucciones:

**Manuscrito:** El manuscrito completo, incluyendo las leyendas y referencias deberán estar escritos a maquina a doble espacio y por un solo lado de cada página, en **TRIPLICADO** y con amplio margen. En página separada deberá incluirse lo siguiente: título, nombre del autor(es) y su grado (ej: MD, FACP), ciudad donde se hizo el trabajo, el hospital o institución académica, patrocinadores del estudio, y si un artículo ha sido leído en alguna reunión o congreso, así debe hacerse constar como una nota al calce.

El manuscrito debe comenzar con una breve introducción en la cual se especifique el propósito del mismo. Las secciones principales (como por ejemplo: materiales y métodos) deben identificarse como un encabezamiento al centro y en letras mayúsculas.

Artículos referentes a resultados de estudios clínicos o investigaciones de laboratorio deben organizarse bajo los siguientes encabezamientos: Introducción, Materiales y Métodos, Resultados, Discusión, Resumen (en español e inglés), Reconocimiento y Referencias.

Artículos referentes a estudios de casos aislados deben organizarse en la siguiente forma: Introducción, Materiales y Métodos si es aplicable, Observaciones del Caso, Discusión, Resumen (en español e inglés), Reconocimientos y Referencias.

**Nomenclatura:** Deben usarse los nombres genéricos de los medicamentos. Podrán usarse también los nombres comerciales, entre paréntesis, si así se desea. Se usará con preferencia el sistema métrico de pesos y medidas.

**Tablas:** Las tablas deben aparecer en hojas separadas. Estas deben incluir el título y el número de la tabla (romano). Los símbolos de unidades deben limitarse al encabezamiento de las columnas. Se deben omitir líneas verticales y horizontales en la tabla.

**Figuras:** Las fotografías y microfotografías se someterán como copias en papel de lustre, sin montar. En el reverso de la figura debe aparecer el número de la figura (arábigo) y el autor y debe indicarse la parte superior.

**Referencias:** Las referencias deben ser numeradas sucesivamente de acuerdo con su aparición en el texto. Los números deben aparecer en paréntesis al nivel de la línea u oración. Al final de cada artículo las referencias deben aparecer en el orden numérico en que se citan en el texto. Estas deben seguir el estilo o patrón del "Index Medicus", el cual se describe a continuación:

Para artículos de Revista:

Apellido(s), e iniciales del autor(es), nombre de la revista, volumen, primera página y año.

Koppisch E.: Bol Asoc Med P Rico 46: 505, 1954.

Para citación de Libros

Apellido(s), e iniciales del autor(es), título, edición, casa editora, ciudad, año y página.

Wintrobe MM: Clinical Hematology, 3rd Ed Lea and Febiger, Philadelphia 1952 p. 67.

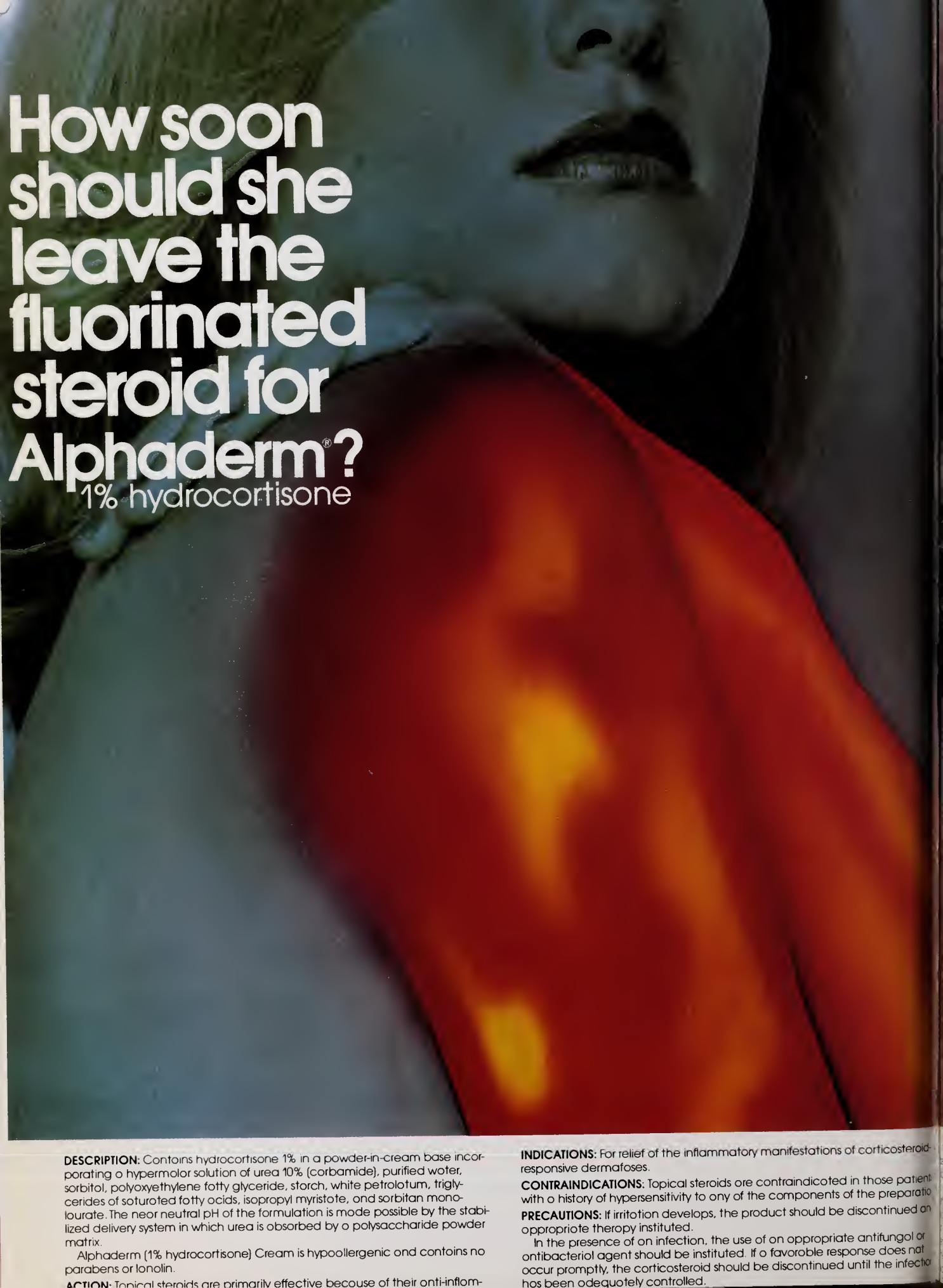
Más de tres autores añadir: et al.

Deben usarse solamente las abreviaturas indicadas en el "Cumulative Index Medicus" que publica la Asociación Médica Americana.

Como guía de referencia para preparar su artículo puede usar la publicación Advice to Authors que publica la Scientific Publications Division, American Medical Association, 535 N Dearborn Street, Chicago, Illinois, 60610.

## Instructions to Authors

The Boletín will accept for publication contributions relating to the various areas of medicine, surgery and allied medical sciences. Special articles and correspondence on subjects of general interest to physicians will also be accepted. All material is accepted with the



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extensive areas are treated or if the occlusive technique is used, there will be increased systemic absorption of the corticosteroid and suitable precautions should be taken, particularly in children and infants.

Although topical steroids have not been reported to have an adverse effect on human pregnancy, the safety of their use in pregnant women has not absolutely been established. In laboratory animals, increases in incidence of fetal abnormalities have been associated with exposure of gestating females to topical corticosteroids, in some cases of rather low dosage levels. Therefore, drugs of this class should not be used extensively on pregnant patients, in large amounts, or for prolonged periods of time. This product is not for ophthalmic use.

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understanding that it is to be published solely in this journal.

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The manuscript should start with a brief introductory paragraph or paragraphs which should state its purpose. The main sections (for example, Materials and Methods) should be identified by center headings in capital letters.

Articles reporting the results of clinical studies or laboratory investigation should be organized under the following headings: Introduction, Material and Methods, Results if indicated, Discussion, Summary in English and Spanish, Acknowledgments if any, and References.

**Nomenclature:** Generic names of drugs should be used; trade names may also be given in parenthesis, if desired. Metric units of measurements should be used preferentially.

**Tables:** These should be typed on separate sheets with the title and table number (Roman) centered. Symbol for units should be confined to the column headings. Vertical and horizontal lines

should be omitted.

**Figures:** Photographs and photomicrographs should be submitted as glossy prints, unmounted. They should be labeled in the back with the name of the authors and figure number (Arabic) and the top should be indicated. Legends to the figures should be typed on a separate sheet.

**References:** These should be numbered serially as they appear in the text. The number should be enclosed in parenthesis on the line of writing and not as superscript numbers. At the end of the article references should be listed in the numerical order in which they are first cited in the text. This list should conform to the Style of the Index Medicus and should be punctuated as in the following examples.

For journal articles:

Surname and initials of author(s), name of journal, volume, first page and year.

Koppisch E: *Bol Asoc Med P Rico* 46: 505, 1954.

For Books:

Surname and initials of author(s), title, edition, publishing house, City, year and page.

Wintrobe MM: *Clinical Hematology*, 3rd Ed Lea and Febiger, Philadelphia 1952 p 67.

More than three authors add: et al.

Abbreviations will conform to those used in the Cumulative Index Medicus, published by the American Medical Association.

For aid in preparing your manuscript refer to the publication Advice to Authors available from the Scientific Publications Division, American Medical Association, 535 N Dearborn St., Chicago, Illinois 60610.

# Health and Safety Tip

From the American Medical Association

535 North Dearborn Street/Chicago, Illinois 60610

## Many Human Organs Can Help Others Live

### Give Body To Others

The human body is a storehouse of human tissue valuable for transplantation, medical education, research and therapy. A person willing to donate all or part of his body after death for one of these purposes is making a generous contribution to society.

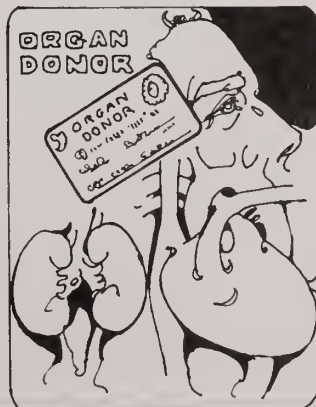
The American Medical Association frequently is asked: "How can I leave my body to help others?"

Actually, it isn't difficult. The Uniform Anatomical Gift Act now adopted by all 50 states and the District of Columbia provides that any person 18 or over may donate all or part of his body after death for research, transplantation or placement in a tissue bank. The donor's wish may be expressed in a written document, often incorporated into his will. His intent should be made known to friends and relatives who will make certain that his wishes are carried out.

Many individuals carry in wallet or purse a small card which states that the bearer wishes to make an anatomical gift after death. The donation is effective only after death. And the doctor who will handle the donated organ cannot be the one who pronounces death. No money can be exchanged in making an anatomical donation. Expenses for funeral arrangements and care of the body after removal of tissues and organs are the responsibility of the donor and his family.

Organs and/or bodies are accepted on a need basis. No medical facility is obliged to accept an offered gift. There may be periods in which the local medical school actually has a surplus of bodies for anatomy studies. And at other times there may be an acute shortage.

Kidneys are routinely transplanted in more than 2,000 individuals each year and more could be used if they were available. Corneas of the eye may be transplanted to restore sight in many persons. Many structural tissues, including bone, tendons, heart valves, fibrous tissues that cover the muscles, and cartilage have been transplanted with success. These tissues can be stored until needed.



September, 1979  
Frank Chappell  
Science News Editor  
AMA

## AVISO DE INTERES

La Junta Editora, consciente de su responsabilidad de hacer que el "Boletín" cumpla a cabalidad con su cometido de divulgar conocimientos médicos, elevar las normas de educación médica y al propio tiempo de llenar las necesidades de todos los compañeros médicos, ha acordado establecer una nueva Sección que se conocerá como "Sección de Preguntas".

Bajo esta nueva Sección, todos los compañeros tendrán la oportunidad de enviarnos preguntas médicas de casos difíciles o casos clínicos para opinión experta. Estas preguntas, con sus respuestas, serán publicadas en esta nueva Sección.

Las preguntas deberán ser enviadas a:

Boletín de la AMPR  
Sección de Preguntas  
Apartado 9387  
Santurce, P. R. 00908

Esperamos sus preguntas.

Juan M. Aranda, MD  
Presidente  
Junta Editora

# Librax®

Each capsule contains 5 mg chlordiazepoxide HCl and 2.5 mg clidinium Br  
**Please consult complete prescribing information, a summary of which follows:**

**Indications:** Based on a review of this drug by the National Academy of Sciences—National Research Council and/or other information, FDA has classified the indications as follows: "Possibly" effective: as adjunctive therapy in the treatment of peptic ulcer and in the treatment of the irritable bowel syndrome (irritable colon, spastic colon, mucous colitis) and acute enterocolitis. Final classification of the less-than-effective indications requires further investigation.

**Contraindications:** Glaucoma; prostatic hypertrophy, benign bladder neck obstruction; hypersensitivity to chlordiazepoxide HCl and/or clidinium Br.

**Warnings:** Caution patients about possible combined effects with alcohol and other CNS depressants, and against hazardous occupations requiring complete mental alertness (e.g., operating machinery, driving). Physical and psychological dependence rarely reported on recommended doses, but use caution in administering Librium® (chlordiazepoxide HCl/Roche) to known addiction-prone individuals or those who might increase dosage, withdrawal symptoms (including convulsions) reported following discontinuation of the drug.

**Usage in Pregnancy:** Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy. Advise patients to discuss therapy if they intend to or do become pregnant.

As with all anticholinergics, inhibition of lactation may occur.

**Precautions:** In elderly and debilitated, limit dosage to smallest effective amount to preclude ataxia, oversedation, confusion (no more than 2 capsules/day initially; increase gradually as needed and tolerated). Though generally not recommended, if combination therapy with other psychotropics seems indicated, carefully consider pharmacology of agents, particularly potentiating drugs such as MAO inhibitors, phenothiazines. Observe usual precautions in presence of impaired renal or hepatic function. Paradoxical reactions reported in psychiatric patients. Employ usual precautions in treating anxiety states with evidence of impending depression; suicidal tendencies may be present and protective measures necessary. Variable effects on blood coagulation reported very rarely in patients receiving the drug and oral anticoagulants, causal relationship not established.

**Adverse Reactions:** No side effects or manifestations not seen with either compound alone reported with Librax. When chlordiazepoxide HCl is used alone, drowsiness, ataxia, confusion may occur, especially in elderly and debilitated, avoidable in most cases by proper dosage adjustment, but also occasionally observed at lower dosage ranges. Syncope reported in a few instances. Also encountered: isolated instances of skin eruptions, edema, minor menstrual irregularities, nausea and constipation, extrapyramidal symptoms, increased and decreased libido—all infrequent, generally controlled with dosage reduction; changes in EEG patterns may appear during and after treatment; blood dyscrasias (including agranulocytosis), jaundice, hepatic dysfunction reported occasionally with chlordiazepoxide HCl, making periodic blood counts and liver function tests advisable during protracted therapy. Adverse effects reported with Librax typical of anticholinergic agents, i.e., dryness of mouth, blurring of vision, urinary hesitancy, constipation. Constipation has occurred most often when Librax therapy is combined with other spasmolytics and/or low residue diets.



Roche Products Inc.  
Manatí, Puerto Rico 00701



In irritable  
bowel syndrome\*



Adjunctive  
**Librax**<sup>®</sup>

Each capsule contains  
5 mg chlordiazepoxide HCl (LIBRIUM<sup>®</sup>)  
and 2.5 mg clidinium Br (QUARZAN<sup>®</sup>).

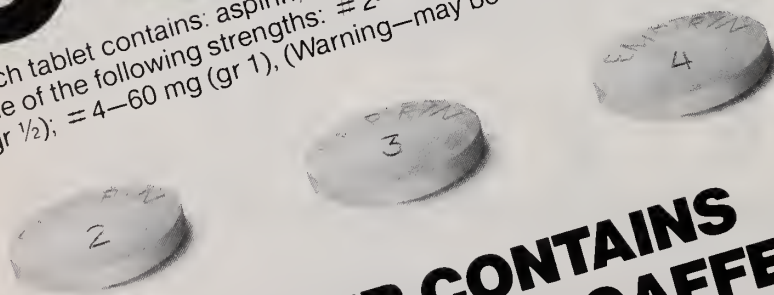
antianxiety/antispasmodic/antimotility

ROCHE

\*Librax has been evaluated as possibly effective for this indication.  
Please see brief summary of prescribing information on preceding page.

# ~~EMPIRIN<sup>®</sup>~~ ~~COMPOUND~~ ~~CODEINE~~ IS NOW ~~EMPIRIN<sup>®</sup>~~ ~~CODEINE~~

Each tablet contains: aspirin, 325 mg; plus codeine phosphate in one of the following strengths:  $\approx 2-15$  mg (gr  $\frac{1}{4}$ );  $\approx 3-30$  mg (gr  $\frac{1}{2}$ );  $\approx 4-60$  mg (gr 1), (Warning—may be habit-forming)



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# BOLETIN

## ASOCIACION MEDICA DE PUERTORICO

### CONTENIDO

SURGICAL MANAGEMENT OF HEPATIC CYSTS

PSIQUIATRIA — 1979

TUBERCULOSIS: CONCEPTOS ACTUALES - PARTE II

DISCURSO DEL DR. GERARDO SANZ ORTEGA - TOMA  
DE POSESION COMO PRESIDENTE DE LA AMPR  
10 DE NOVIEMBRE DE 1979

NOTA BIOGRAFICA: DR. GERARDO SANZ ORTEGA

PENSAMIENTO EN LA EPOCA NAVIDEÑA:  
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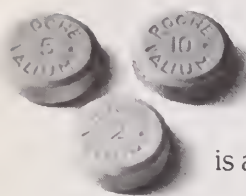
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# A character all its own.



Valium (diazepam/Roche) is a benzodiazepine with a character all its own.

Pharmacologically, it is a potent skeletal muscle relaxant and anticonvulsant (in adjunctive use), as well as an antianxiety agent. Pharmacokinetically, only Valium provides active diazepam as well as the active metabolites 3-hydroxydiazepam, desmethyldiazepam and oxazepam.

But the individual character of Valium is even more apparent clinically than pharmacokinetically. And far more significant. That's because of the patient response obtained with Valium. A response which brings a calmer frame of mind. A response which has a pronounced effect on the somatic symptoms of anxiety, particularly muscular tension. A response which helps the patient feel more like himself again because of the way Valium reduces the overwhelming symptoms of anxiety and psychic tension.

Another important aspect of the clinical character of Valium is safety. Though drowsiness, ataxia and fatigue are possible, these and more serious side effects are rarely a problem. Of course, as with all CNS-acting drugs, patients taking Valium should be cautioned against driving, operating dangerous machinery or the simultaneous ingestion of alcohol.

Unquestionably, many psychotherapeutic agents, including other benzodiazepines, have antianxiety effects. But one fact remains: you get a certain kind of patient response with Valium. It's a response you want. A response you know. A response you trust as part of your overall management of anxiety and psychic tension.

**Valium<sup>®</sup> <sup>IV</sup>**  
**diazepam/Roche**  
2-mg, 5-mg, 10-mg scored tablets  
**a prudent choice in psychic  
tension and anxiety**

**Before prescribing, please consult complete product information, a summary of which follows:**

**Indications:** Tension and anxiety states; somatic complaints which are concomitants of emotional factors; psychoneurotic states manifested by tension, anxiety, apprehension, fatigue, depressive symptoms or agitation; symptomatic relief of acute agitation, tremor, delirium tremens and hallucinosis due to acute alcohol withdrawal; adjunctively in skeletal muscle spasm due to reflex spasm to local pathology; spasticity caused by upper motor neuron disorders; athetosis; stiff-man syndrome; convulsive disorders (not for sole therapy).

The effectiveness of Valium (diazepam/Roche) in long-term use, that is, more than 4 months, has not been assessed by systematic clinical studies. The physician should periodically reassess the usefulness of the drug for the individual patient.

**Contraindicated:** Known hypersensitivity to the drug. Children under 6 months of age. Acute narrow angle glaucoma; may be used in patients with open angle glaucoma who are receiving appropriate therapy.

**Warnings:** Not of value in psychotic patients. Caution against hazardous occupations requiring complete mental alertness. When used adjunctively in convulsive disorders, possibility of increase in frequency and/or severity of grand mal seizures may require increased dosage of standard anticonvulsant medication; abrupt withdrawal may be associated with temporary increase in frequency and/or severity of seizures. Advise against simultaneous ingestion of alcohol and other CNS depressants. Withdrawal symptoms (similar to those with barbiturates and alcohol) have occurred following abrupt discontinuance (convulsions, tremor, abdominal and muscle cramps, vomiting and sweating). Keep addiction-prone individuals under careful surveillance because of their predisposition to habituation and dependence.

**Usage in Pregnancy: Use of minor tranquilizers during first trimester should almost always be avoided because of increased risk of congenital malformations as suggested in several studies. Consider possibility of pregnancy when instituting therapy; advise patients to discuss therapy if they intend to or do become pregnant.**

**Precautions:** If combined with other psychotropics or anticonvulsants, consider carefully pharmacology of agents employed; drugs such as phenothiazines, narcotics, barbiturates, MAO inhibitors and other antidepressants may potentiate its action. Usual precautions indicated in patients severely depressed, or with latent depression, or with suicidal tendencies. Observe usual precautions in impaired renal or hepatic function. Limit dosage to smallest effective amount in elderly and debilitated to preclude ataxia or oversedation.

**Side Effects:** Drowsiness, confusion, diplopia, hypotension, changes in libido, nausea, fatigue, depression, dysarthria, jaundice, skin rash, ataxia, constipation, headache, incontinence, changes in salivation, slurred speech, tremor, vertigo, urinary retention, blurred vision. Paradoxical reactions such as acute hyperexcited states, anxiety, hallucinations, increased muscle spasticity, insomnia, rage, sleep disturbances, stimulation have been reported; should these occur, discontinue drug. Isolated reports of neutropenia, jaundice; periodic blood counts and liver function tests advisable during long-term therapy.

**Dosage:** Individualize for maximum beneficial effect. *Adults:* Tension, anxiety and psychoneurotic states, 2 to 10 mg b.i.d. to q.i.d.; alcoholism, 10 mg t.i.d. or q.i.d. in first 24 hours, then 5 mg t.i.d. or q.i.d. as needed; adjunctively in skeletal muscle spasm, 2 to 10 mg t.i.d. or q.i.d.; adjunctively in convulsive disorders, 2 to 10 mg b.i.d. to q.i.d. *Geriatric or debilitated patients:* 2 to 2½ mg, 1 or 2 times daily initially, increasing as needed and tolerated. (See Precautions.) *Children:* 1 to 2½ mg t.i.d. or q.i.d. initially, increasing as needed and tolerated (not for use under 6 months).

**Supplied:** Valium<sup>®</sup> (diazepam) Tablets, 2 mg, 5 mg and 10 mg—bottles of 100 and 500; Tel-E-Dose<sup>®</sup> packages of 100, available in trays of 4 reverse-numbered boxes of 25, and in boxes containing 10 strips of 10; Prescription Paks of 50, available singly and in trays of 10.



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# The heart of the matter in hypertension is the kidney

The kidney—not the heart—is the key to long-term arterial pressure control. Diuretics help the kidney excrete sodium, reduce fluid volume and lower blood pressure.

No diuretic blocks sodium retention longer than Hygroton.

In mild hypertension low-dose Hygroton 25 mg. An effective, conservative therapy.

## In mild hypertension

Low-dose

# Hygroton<sup>®</sup> 25 mg. one a day

## (chlorthalidone USP)

## Gets to the heart of the matter... simply

### BRIEF SUMMARY

**Indications:** Hypertension, adjunctive therapy in edema.

**Contraindications:** Anuria, hypersensitivity to chlorthalidone or other sulfonamide-derived drugs.

**Warnings:** Should be used with caution in severe renal disease, impaired hepatic function or progressive liver disease. May add to or potentiate the action of other antihypertensive drugs. Sensitivity reactions may occur in patients with a history of allergy or bronchial asthma. There is a possibility of exacerbation or activation of systemic lupus erythematosus with thiazides, which are related to chlorthalidone. This has not been reported with chlorthalidone. Thiazides cross the placental barrier and appear in cord blood. Use in pregnant women requires that the anticipated benefits of the drug be weighed against possible hazards to the fetus. These hazards include fetal or neonatal jaundice, thrombocytopenia, and possibly other adverse reactions which have occurred in the adult. In nursing mothers, thiazides cross the placental barrier and appear in breast milk. If use of the drug is essential, the patient should stop nursing.

**Precautions:** Periodic determination of serum electrolytes to detect possible electrolyte imbalance should be performed at appropriate intervals. All patients receiving chlorthalidone should be observed for clinical signs of fluid or electrolyte imbalance, namely, hyponatremia, hypochloremic alkalosis, and hypokalemia. Serum and urine electrolyte determinations are particularly important when the patient is vomiting excessively or receiving parenteral fluids. Medication such as digitalis may also influence serum electrolytes. Hypokalemia may develop with chlorthalidone as with any other potent diuretic, especially with brisk diuresis, when severe cirrhosis is present, or during concomitant use of corticosteroids or ACTH. Interference with adequate oral electrolyte intake will also contribute to hypokalemia. Digitalis therapy may exaggerate metabolic effects of hypokalemia especially with reference to myocardial activity. Any chloride deficit is generally mild and usually does not require specific treatment except under extraordinary circumstances (as in liver disease or renal disease). Dilutional hyponatremia may occur in edematous

patients in hot weather. Hypernatremia may occur or be precipitated in certain patients. Insulin requirements in diabetic patients may be increased, decreased, or unchanged and latent diabetes mellitus may become manifest. Chlorthalidone and related drugs may increase the responsiveness to tubocurarine. The antihypertensive effects of the drug may be enhanced in the postsympathectomy patient. Chlorthalidone and related drugs may decrease arterial responsiveness to norepinephrine. If progressive renal impairment becomes evident, as indicated by a rising nonprotein nitrogen or blood urea nitrogen, a careful reappraisal of therapy is necessary with consideration given to withholding or discontinuing diuretic therapy. Chlorthalidone and related drugs may decrease serum BUN levels without signs of fluid disturbance.

**Adverse Reactions:** Anorexia, gastric irritation, nausea, vomiting, cramping, diarrhea, constipation, jaundice (intrahepatic cholestatic jaundice), pancreatitis, dizziness, vertigo, paresthesias, headache, xanthopsia; leukopenia, agnucytosis, thrombocytopenia, aplastic anemia; purpura, photosensitivity, rash, urticaria, necrotizing angitis (vasculitis) (cutaneous vasculitis), Lyell's syndrome (toxic epidermal necrolysis). Orthostatic hypotension may occur and may be aggravated by alcohol, barbiturates or narcotics. Other adverse reactions include hyperglycemia, glycosuria, hypouricemia, muscle spasm, weakness, restlessness, impotence. Whenever adverse reactions are moderate to severe, chlorthalidone dosage should be reduced or therapy withdrawn.

**Usual Dose:** One tablet daily.

**How Supplied:** Tablets—100 mg. (white, scored), 50 mg. (aqua) and 25 mg. (parch) in bottles of 100 and 1000; unit-dose blister packs, boxes of 100 (10 x 10 strips). Also, 100 mg. and 50 mg. in PAKs of 28 tablets, boxes of 5.

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Manati, P.R. 00701





# Announcing a theophylline tha

## Convenient q12h dosage provides 24-hour relief of bronchospasm

Sustained, therapeutic serum levels are achieved with q12h dosage.


**Simple, single-entity therapy.**

Sustaire contains only one active ingredient — anhydrous theophylline, specially formulated to provide uninterrupted relief of bronchospasm.

Unlike short-acting bronchodilators, Sustaire (theophylline, anhydrous) helps avoid the potentially toxic peaks and subtherapeutic valleys that interfere with continuous therapy.

**Improved compliance stems from improved convenience of the q12h**





works all day...and all night

SUSTAINED RELEASE

**SUSTAIRE<sup>®</sup>**

theophylline (anhydrous) 100 mg  
300 mg  
Scored  
Tablets

For Sustaire prescribing information, including adverse reactions and contraindications, please see last page of this advertisement.

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# Sustained Release

# SUSTAIRE®

100 mg  
300 mg  
Scored  
Tablets

## theophylline(anhydrous)

## A THEOPHYLLINE THAT WORKS ALL DAY...AND ALL NIGHT

### PRESCRIBING INFORMATION

#### SUSTAIRE® theophylline (anhydrous) U.S.P. SUSTAINED RELEASE TABLETS

**DESCRIPTION:** SUSTAIRE Sustained Release Tablets contain not less than 94.0 percent and not more than 106.0 percent of the labeled amount of C<sub>7</sub>H<sub>8</sub>N<sub>4</sub>O<sub>2</sub>. Theophylline, a xanthine compound, is a white, odorless crystalline powder, having a bitter taste. SUSTAIRE contains anhydrous theophylline.

**CLINICAL PHARMACOLOGY:** Theophylline directly relaxes the smooth muscle of the bronchial airways and pulmonary blood vessels, thus acting mainly as a bronchodilator, diuretic, cardiac stimulant, cerebral stimulant and skeletal muscle stimulant. The actions of theophylline may be mediated through inhibition of phosphodiesterase and a resultant increase in intracellular cyclic AMP which could mediate smooth muscle relaxation. At concentrations higher than attained *in vivo*, theophylline also inhibits the release of histamine by mast cells.

SUSTAIRE has been specifically formulated, clinically tested, and shown to provide a therapeutically effective serum level when administered on a q12h dosage schedule. SUSTAIRE minimizes the peaks and valleys of serum levels commonly found with shorter-acting theophylline products.

*In vitro*, theophylline has been shown to react synergistically with beta agonists that increase intracellular cyclic AMP through the stimulation of adenylyl cyclase (isoproterenol), but synergism has not been demonstrated in patient studies and more data is needed to determine if theophylline and beta agonists have clinically important additive effect *in vivo*.

Apparently, no development of tolerance occurs with chronic use of theophylline. The half-life is shortened with cigarette smoking. The half-life is prolonged in alcoholism, reduced hepatic or renal function, congestive heart failure, and in patients receiving antibiotics such as TAO (troleandomycin), erythromycin and clindamycin. High fever for prolonged periods may decrease theophylline elimination.

#### THEOPHYLLINE ELIMINATION CHARACTERISTICS

	Theophylline Clearance Rates (mean ± S.D.)	Half-life Average (mean ± S.D.)
Children (over 6 months of age):	1.45 ± .58 ml/kg/min	3.7 ± 1.1 hours
Adult nonsmokers with uncomplicated asthma	.65 ± .19 ml/kg/min	8.7 ± 2.2 hours

Newborn infants have extremely slow clearances and half-lives exceeding 24 hours which approach those seen for older children after about 3-6 months.

Older adults with chronic obstructive pulmonary disease, any patients with cor pulmonale or other causes of heart failure, and patients with liver pathology may have much lower clearances with half-lives that may exceed 24 hours.

The half-life of theophylline in smokers (1 to 2 packs/day) averaged 4-5 hours among various studies, much shorter than the half-life in non-smokers who averaged about 7-9 hours. The increase in theophylline clearance caused by smoking is probably the result of induction of drug-metabolizing enzymes that do not readily normalize after cessation of smoking. It appears that between 3 months and 2 years may be necessary for normalization of the effect of smoking on theophylline pharmacokinetics.

**INDICATIONS:** For relief and/or prevention of symptoms from asthma and reversible bronchospasm associated with chronic bronchitis and emphysema.

**CONTRAINDICATIONS:** In individuals who have shown hypersensitivity to any of its components.

**WARNINGS:** Status asthmaticus is a medical emergency. Optimal therapy frequently requires additional medication including corticosteroids when the patient is not rapidly responsive to bronchodilators.

Excessive theophylline doses may be associated with toxicity, and serum theophylline levels are recommended to assure maximal benefit without excessive risk. Incidence of toxicity increases at levels greater than 20 mcg/ml. Morphine, curare, and stilbamidine should be used with caution in patients with airflow obstruction since they stimulate histamine release and can induce asthmatic attacks. They may also suppress respiration leading to respiratory failure. Alternative drugs should be chosen whenever possible.

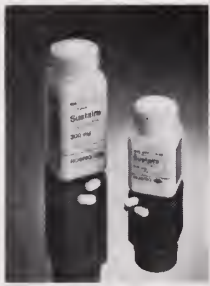
There is an excellent correlation between high blood levels of theophylline resulting from conventional doses and associated clinical manifestations of toxicity in (1) patients with lowered body plasma clearances (due to transient cardiac decompensation), (2) patients with liver dysfunction or chronic obstructive lung disease, (3) patients who are older than 55 years of age, particularly males.

There are often no early signs of less serious theophylline toxicity such as nausea and restlessness, which may appear in up to 50 percent of patients prior to onset of convulsions. Ventricular arrhythmias or seizures may be the first signs of toxicity.

Many patients who have higher theophylline serum levels exhibit a tachycardia. Theophylline products may worsen pre-existing arrhythmias.

**USAGE IN PREGNANCY:** Safe use in pregnancy has not been established relative to possible adverse effects on fetal development, but neither have adverse effects on fetal development been established. This is, unfortunately, true for most antiasthmatic medications. Therefore, use of theophylline in pregnant women should be balanced against the risk of uncontrolled asthma.

**PRECAUTIONS:** Mean half-life is shorter in smokers than in non-smokers, therefore, smokers may require larger doses of theophylline. Theophylline should not be administered concurrently with other xanthine medications. Use with caution in patients with severe cardiac disease, severe hypoxemia, hypertension, hyperthyroidism, acute myocardial injury, cor pulmonale, congestive heart failure, liver disease, and in the elderly (especially males), and in neonates. Great caution should especially be used in giving theophylline to patients in congestive heart failure. Such pa-



tients have shown markedly prolonged theophylline blood level curves with theophylline persisting in serum for long periods following discontinuation of the drug.

Use theophylline cautiously in patients with history of peptic ulcer. Theophylline may occasionally act as a local irritant to G.I. tract although gastrointestinal symptoms are more commonly central and associated with serum concentrations over 20 mcg/ml.

**ADVERSE REACTIONS:** The most consistent adverse reactions are usually due to overdose and are:

1. Gastrointestinal—nausea, vomiting, epigastric pain, hematemesis, diarrhea.
2. Central nervous system—headaches, irritability, restlessness, insomnia, reflex hyperexcitability, muscle twitching, clonic and tonic generalized convulsions.
3. Cardiovascular—palpitation, tachycardia, extrasystoles, flushing, hypotension, circulatory failure, life threatening ventricular arrhythmias.
4. Respiratory—tachypnea.
5. Renal—albuminuria, increased excretion of renal tubular cells and red blood cells; potentiation of diuresis.
6. Others—hyperglycemia and inappropriate ADH syndrome.

**DRUG INTERACTIONS:** Toxic synergism with ephedrine has been documented and may occur with some sympathomimetic bronchodilators.

Drug	Effect
Aminophylline with Lithium Carbonate	Increased excretion of Lithium Carbonate
Aminophylline with Propranolol	Antagonism of Propranolol effect
Theophylline with Furosemide	Increased Diuresis of Furosemide
Theophylline with Hexamethonium	Decreased Hexamethonium-induced chronotropic effect
Theophylline with Reserpine	Reserpine-induced Tachycardia
Theophylline with Chlorthalidopoxide	Chlorthalidopoxide-induced fatty acid mobilization
Theophylline with Cyclamycin, TAO (troleandomycin), Erythromycin, Lincomycin	Increased Theophylline plasma levels

#### OVERDOSAGE: Management.

- A. If potential oral overdose is established and seizure has not occurred:
  - 1) Induce vomiting.
  - 2) Administer a cathartic (this is particularly important if sustained release preparations have been taken).
  - 3) Administer activated charcoal.
- B. If patient is having a seizure:
  - 1) Establish an airway.
  - 2) Administer O<sub>2</sub>.
  - 3) Treat the seizure with intravenous diazepam, 0.1 to 0.3 mg/kg up to 10 mg.
  - 4) Monitor vital signs, maintain blood pressure and provide adequate hydration.
- C. Post-Seizure Coma:
  - 1) Maintain airway and oxygenation.
  - 2) If a result of oral medication, follow above recommendations to prevent absorption of drug, but intubation and lavage will have to be performed instead of inducing emesis, and the cathartic and charcoal will need to be introduced via a large bore gastric lavage tube.
  - 3) Continue to provide full supportive care and adequate hydration while waiting for drug to be metabolized. In general, the drug is metabolized sufficiently rapidly so as to not warrant consideration of dialysis.
- D. Animal studies suggest that phenobarbital may decrease theophylline toxicity. There is as yet, however, insufficient data to recommend pre-treatment of an overdose with phenobarbital.

**DOSAGE AND ADMINISTRATION:** Therapeutic serum levels associated with optimal likelihood for benefit and minimal risk of toxicity are considered to be between 10 mcg/ml and 20 mcg/ml. Levels above 20 mcg/ml may produce toxic effects. There is great variation from patient to patient in dosage needed in order to achieve a therapeutic blood level because of variable rates of elimination. Because of this wide variation from patient to patient, and the relatively narrow therapeutic blood level range, dosage must be individualized and monitoring of theophylline serum levels is highly recommended.

Dosage should be calculated on the basis of lean (ideal) body weight where mg/kg doses are stated. Theophylline does not distribute into fatty tissue.

Giving theophylline with food may prevent the rare case of stomach irritation; and though absorption may be slower, it is still complete.

**Usual Initial Dose:** The average initial children's (under 9 years of age) dose is one SUSTAIRE (theophylline, anhydrous) 100 mg tablet q12h.

The average initial children's (ages 9-12) dose is one-half (150 mg) of a SUSTAIRE 300 mg tablet q12h.

The average initial adolescent (ages 12-16) dose is two SUSTAIRE 100 mg tablets q12h.

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Adults	13 mg per day	6.5 mg q12h

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- \* **Surgical Management of Hepatic Cysts** ..... 455  
*Norma I. Cruz, MD and Enrique Vázquez Quintana, MD*

Hepatic cysts are usually classified as parasitic or non parasitic. Echinococcus and Entamoeba histolitica are the most frequent organisms responsible for the former. The non parasitic hepatic cysts are usually congenital or secondary to trauma, infection or neoplastic processes. In this article Cruz and Vázquez Quintana presents a patient with what appears to be a congenital solitary hepatic cyst. They make an excellent review of the diagnostic classification of hepatic cysts and suggest different modalities of treatment. This article should be of interest to all of our readers.

- \* **Psiquiatría: 1979** ..... 459  
*Néctar de la R. de Torregrosa, MD*

En esta comunicación la autora resume la posición actual de la psiquiatría en la medicina. Presenta en forma concisa y sistemática la evolución del sicoanálisis y la farmacoterapia. Al comenzar la década del ochenta, la psiquiatría se ha diversificado en psiquiatría clínica general, psiquiatría de niños y adolescentes, psiquiatría forense, de familia de comunidad y biopsiquiatría. Cada una de estas subdivisiones tiene características propias relacionadas a la población que sirve, métodos diagnósticos y modalidades de tratamientos disponibles.

- \* **Tuberculosis: Conceptos Actuales - Parte II** ..... 463  
*Ramón Ramírez Ronda, MD y Carlos H. Ramírez Ronda, MD, FACP*

En la segunda parte de "Conceptos Actuales de Tuberculosis", los autores definen y resumen las indicaciones para quimioterapia clásica, bifásica, intermitente y de corta duración. Discuten ellos el período de infectividad de un paciente con tuberculosis activa al igual que las indicaciones actuales para tener al paciente hospitalizado. Como regla general la hospitalización de pacientes con tuberculosis pulmonar depende de la condición médica general del paciente. El momento en donde estos pacientes se convierten en no infecciosos está relacionado con la susceptibilidad del microorganismo a las drogas, y probablemente ocurre cerca o inmediatamente después de instituir el tratamiento. Se enfatiza que el éxito del control moderno de la tuberculosis depende mayormente de programas ambulatorios adecuados para el tratamiento y seguimiento clínico de estos pacientes.

- \* **Discurso Pronunciado por el Dr. Gerardo Sanz Ortega al tomar Posesión como Presidente de la AMPR el 10 de noviembre de 1979** ..... 474

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In therapy of skin and skin structure infections  
due to susceptible strains of staphylococci and/or streptococci...

# THE FIRST ORAL CEPHALOSPORIN THAT WORKS NIGHT AND DAY ON A SINGLE DOSE



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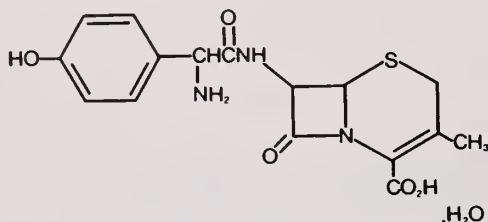
# DURICEF<sup>®</sup>

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1. Data on file, Mead Johnson Pharmaceutical Division.
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**DESCRIPTION:** DURICEF<sup>®</sup> (cefadroxil monohydrate) is a semisynthetic cephalosporin antibiotic intended for oral administration. It is a white to yellowish-white crystalline powder. It is soluble in water and it is acid-stable. It is chemically designated as 7-[[D-2-amino-2-(4-hydroxyphenyl)acetyl]amino]-3-methyl-8-oxo-5-thia-1-azabicyclo [4.2.0]oct-2-ene-2-carboxylic acid monohydrate. It has the following structural formula:



**Clinical Pharmacology**—DURICEF (cefadroxil monohydrate) is rapidly absorbed after oral administration. Following single doses of 500 and 1000 mg., average peak serum concentrations were approximately 16 and 28 mcg./ml., respectively. Measurable levels were present 12 hours after administration. Over 90 percent of the drug is excreted unchanged in the urine within eight hours. Peak urine concentrations are approximately 1800 mcg./ml. during the period following a single 500 mg. oral dose. Increases in dosage generally produce a proportionate increase in DURICEF urinary concentration. The urine antibiotic concentration, following a 1 gm. dose, was maintained well above the MIC of susceptible urinary pathogens for 20 to 22 hours.

**MICROBIOLOGY:** *In vitro* tests demonstrate that the cephalosporins are bactericidal because of their inhibition of cell-wall synthesis. DURICEF is active against the following organisms *in vitro*:

*Beta-hemolytic streptococci*  
*Staphylococci*, including coagulase-positive, coagulase-negative, and penicillinase-producing strains  
*Streptococcus (Diplococcus) pneumoniae*  
*Escherichia coli*  
*Proteus mirabilis*  
*Klebsiella* species

**Note**—Most strains of *Enterococci* (*Streptococcus faecalis* and *S. faecium*) are resistant to DURICEF. It is not active against most strains of *Enterobacter species*, *P. morganii*, and *P. vulgaris*. It has no activity against *Pseudomonas* or *Herella species*.

**Disc Susceptibility Tests**—Quantitative methods that require measurement of zone diameters give the most precise estimates of antibiotic susceptibility. One recommended procedure (CFR Section 460.1) uses cephalosporin class disc for testing susceptibility; interpretations correlate zone diameters of the disc test with MIC values for DURICEF. With this procedure, a report from the laboratory of "resistant" indicates that the infecting organism is not likely to respond to therapy. A report of "intermediate susceptibility" suggests that the organism would be susceptible if the infection is confined to the urinary tract, as DURICEF produces high antibiotic levels in the urine.

**INDICATIONS:** DURICEF (cefadroxil monohydrate) is indicated for the treatment of the following infections when caused by susceptible strains of the designated microorganisms:

Urinary tract infections caused by *E. coli*, *P. mirabilis*, and *Klebsiella* species  
 Skin and skin structure infections caused by staphylococci and/or streptococci

**Note**—Culture and susceptibility tests should be initiated prior to and during therapy. Renal function studies should be performed when indicated.

**CONTRAINDICATION:** DURICEF (cefadroxil monohydrate) is contraindicated in patients with known allergy to the cephalosporin group of antibiotics.

**WARNING: IN PENICILLIN-ALLERGIC PATIENTS, CEPHALOSPORIN ANTIBIOTICS SHOULD BE USED WITH GREAT CAUTION. THERE IS CLINICAL AND LABORATORY EVIDENCE OF PARTIAL CROSS-ALLERGENICITY OF THE PENICILLINS AND THE CEPHALOSPORINS, AND THERE ARE INSTANCES OF PATIENTS WHO HAVE HAD REACTIONS TO BOTH DRUGS (INCLUDING FATAL ANAPHYLAXIS AFTER PARENTERAL USE.)**

Any patient who has demonstrated a history of some form of allergy, particularly to drugs, should receive antibiotics cautiously and then only when absolutely necessary. No exception should be made with regard to DURICEF (cefadroxil monohydrate).

**PRECAUTIONS:** Patients should be followed carefully so that any side-effects or unusual manifestations of drug idiosyncrasy may be detected. If a hypersensitivity reaction occurs, the drug should be discontinued and the patient treated with the usual agents (e.g., epinephrine or other pressor amines, antihistamines, or corticosteroids).

DURICEF (cefadroxil monohydrate) should be used with caution in the presence of markedly impaired renal function (creatinine clearance rate of less than 50 ml/min/1.73M<sup>2</sup>). (See Dosage and Administration.) In patients with known or suspected renal impairment, careful clinical observation and appropriate laboratory studies should be made prior to and during therapy.

Prolonged use of DURICEF may result in the overgrowth of nonsusceptible organisms. Careful observation of the patient is essential. If superinfection occurs during therapy, appropriate measures should be taken.

Positive direct Coombs tests have been reported during treatment with the cephalosporin antibiotics. In hematologic studies or in transfusion cross-matching procedures when antiglobulin tests are performed on the minor side or in Coombs testing of newborns whose mothers have received cephalosporin antibiotics before parturition, it should be recognized that a positive Coombs test may be due to the drug.

**USAGE IN PREGNANCY:** Although no teratogenic or anti-fertility effects were seen in reproductive studies in mice and rats receiving dosages greater than the normal human dose, the safety of this drug for use in human pregnancy has not been established. The benefits of the drug in pregnant women should be weighed against a possible risk to the fetus.

**ADVERSE REACTIONS:** Gastrointestinal—The most frequent side-effect has been nausea. It was infrequently severe enough to warrant cessation of therapy. Administration with food decreases nausea and does not decrease absorption. Diarrhea and dysuria have also occurred.

**Hypersensitivity**—Allergies (in the form of rash, urticaria, and angioedema) have been observed. These reactions usually subsided upon discontinuation of the drug.

Other reactions have included genital pruritus, genital moniliasis, vaginitis, and moderate transient neutropenia.

**DOSAGE AND ADMINISTRATION:** DURICEF (cefadroxil monohydrate) is acid stable and may be administered orally without regard to meals. Administration with food may be helpful in diminishing potential gastrointestinal complaints occasionally associated with oral cephalosporin therapy.

**Adults**—For urinary tract infections the usual adult dosage is one gm. (two 500 mg. capsules) two times per day. For skin and skin structure infections the usual dose is 500 mg. two times per day or 1 gm. once a day.

In patients with renal impairment, the dosage of cefadroxil should be adjusted according to creatinine clearance rates to prevent drug accumulation. The following schedule is suggested. In adults, the initial dose is 1 gm. of DURICEF (cefadroxil monohydrate) and the maintenance dose (based on the creatinine clearance rate [ml/min/1.73M<sup>2</sup>]) is 500 mg. at the time intervals listed below.

Creatinine Clearances	Dosage Interval
0-10 ml/min	36 hours
10-25 ml/min	24 hours
25-50 ml/min	12 hours

Patients with creatinine clearance rates over 50 ml/min may be treated as if they were patients having normal renal function.

**Children**—Dosage and safety have not yet been established in children.

**HOW SUPPLIED:** DURICEF<sup>®</sup> (cefadroxil monohydrate) capsules 500 mg. for oral administration in an opaque maroon cap and opaque white body No. 0 hard gelatin capsule. On each half capsule printed in black is "MJ" and "500." Available in bottles of 24 capsules (NDC 0087-0784-41) and 100 capsules (NDC 0087-0784-42).

U.S. Patent Re. 29,164

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# SURGICAL MANAGEMENT OF HEPATIC CYSTS

Norma I. Cruz, MD and Enrique Vázquez Quintana, MD

**Summary:** A case is presented of a patient with a congenital solitary hepatic cyst.

The different etiologies responsible for hepatic cysts as well as the indications for surgery in each type are presented. The surgical procedures of choice are discussed.

## Introduction

Hepatic cysts are relatively uncommon in clinical practice, yet their surgical management presents a challenge because no one surgeon has a large experience and few take the time to review the existing literature on the topic, when faced with an isolated case.

It is not a rare experience for the practicing surgeon to have to re-explore a patient with re-accumulation of the cyst fluid, because the initial choice of drainage procedure was inadequate.

The purpose of this paper is to present a simple, systematic approach to this surgical problem; reviewing the different etiologies, and the surgical procedures of choice. Also a case presentation is made.

## Case Presentation

A fifty-four-year-old Puerto Rican female pa-

tient presented in September 1978 at the Methodist Hospital in Brooklyn, with an abdominal mass, she was asymptomatic except for the presence of the enlarged abdominal girth. She had made a trip to Mexico in 1963 but had no history of diarrheas during this time. A sonogram performed showed the entire right lobe of the liver replaced by a sonolucent structure with liquid content. Liver function tests were within normal limits and a renal scan showed good functioning kidneys bilaterally. Indirect hemagglutination titers for amebiasis and *Echinococcus* were both less than 1:32 (diagnostic titers are 1:128). Exploratory laparotomy was performed with drainage of 3 liters of a chocolate-like fluid which on pathological examination was negative for tumor cells or parasites. The patient was discharged home on October 1978. On February 1979, she was admitted to the University of Puerto Rico Hospital because of recurrence of the cyst. A second exploratory laparotomy was performed which revealed a very large solitary cyst projecting over the inferior surface of the right lobe of the liver. Intra operative cholangiogram revealed a communication of the cyst to the biliary system and an internal drainage of the most dependent part of the cyst to a Roux-en-Y jejunal limb was performed. The patient has been asymptomatic for a period of ten months, without evidence of re-accumulation of cyst fluid.

At present we believe this patient had a solitary congenital cyst since there were no other lesions within the hepatic parenchyma and no renal involvement. Though the possibility of this being a variant of polycystic disease can not be fully ruled out, we still think surgery is equally indicated to provide relief from large and symptomatic cystic masses.

## Discussion

Whenever possible a diagnosis should be established, as to the etiology of the cyst be-

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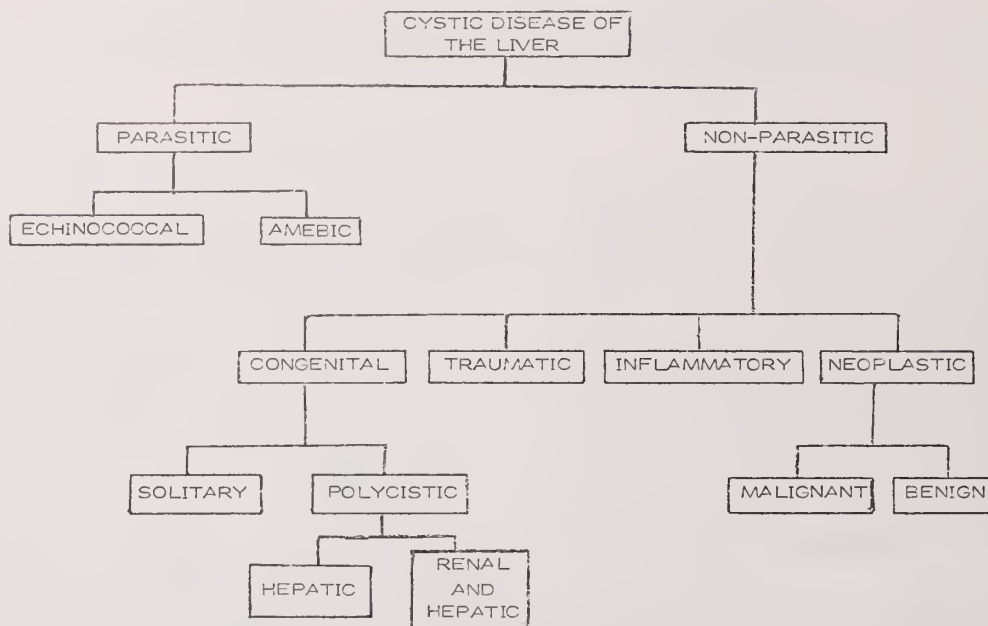


FIGURE 1: CLASSIFICATION OF HEPATIC CYSTIC DISEASE

fore surgery.

Hepatic cysts are classified in two main groups, as either parasitic or non-parasitic (Fig. 1).

Among the parasitic liver cysts the *echinococcal* cysts is the prototype. Patients usually have a history of having visited endemic areas of South America, Eastern Europe, Australia or South Africa. Two forms of the tapeworm, *Echinococcus granulosus* and *Echinococcus multilocularis* produce the disease in man.

The adult form lives in the intestine of the dog from which ova are passed in the stool. These ova are ingested by the intermediate host, usually sheep and cattle, but occasionally man. The chitinous envelope of the ova is dissolved by gastric juice liberating the embryo in the duodenum. The embryos pass into the portal circulation, traveling to the liver which acts as a filter. Lodged in the liver the embryo develops into a cyst which has a characteristic architec-

ture, with an inner germinative layer and a thick outer layer which often calcifies. The cyst is filled with a clear fluid in which daughter cysts and scolices float. The cyst fluid is usually under very high pressure. The diagnosis can be made with the help of serologic tests, such as the indirect hemagglutination test or the complement fixation test and the response to intradermal injection of cyst fluid (Casoni test).

The treatment of echinococcal cysts is surgical removal (4). The cyst is first evacuated with great care through a large bore needle, being aware that the contents of the cyst is under very high pressure. The fluid is replaced with 20 percent hypertonic saline, which is allowed to remain for a few minutes. The use of formalin or absolute alcohol is discouraged because they may cause damage to the biliary tree. The hypertonic saline serves to kill the scolices. Once evacuated, the cyst is excised, using the plane of cleavage between

the thick outer layer and the fibrous adventitia of the adjacent liver. The remaining defect may be packed by a pedicle of omentum.

In England Mebendazole (Vermox R) has been used for the management of Echinococcal cyst without surgery (1, 5, 16) but at present this is not recommended for general use.

The second consideration among the parasitic liver cysts is the *amebic* type. The protozoan parasite *Entamoeba histolytica* is the causative organism. Cysts are passed in the stools of the host and may survive for prolonged periods in moist surroundings. Cysts ingested with fecally contaminated water and food transmit the infection to the new host. The lesions in man are caused by the trophozoite.

It is generally accepted that amebae reach the liver by the portal blood stream from an ulcerated lesion in the bowel wall. The abscess cavity contains liquified and necrotic liver cells having the appearance of "anchovy paste" or "chocolate sauce".

The diagnosis can be made with the help of indirect hemagglutination and complement fixation tests, to detect antibodies to *E. histolytica*. Treatment is medical; (15) Metronidazole (Flagyl) is currently the drug of choice, with a dose of 750 mg. orally, three times daily for 10 days. When evacuation of the abscess becomes necessary because rupture appears imminent, needle aspiration and preliminary administration of metronidazole are the procedures of choice.

The only indication for surgical open drainage of an amebic abscess of the liver is secondary infection which fails to respond to appropriate antibiotic therapy.

The non-parasitic cysts of the liver are currently classified (6) as:

1. Congenital
  - a. Solitary
  - b. Polycystic
2. Traumatic
3. Inflammatory
4. Neoplastic

Of all forms, the *polycystic* type is the most common but it is not a surgical condition, (8) and the management should be conservative (13). Normal hepatic function is preserved over periods of many years despite extensive involvement of the liver (14). The major factor determining prognosis in this patient is the extent of the renal damage. Surgery is indicated only for complications; such as for infection within the cyst, or to reduce the weight of the retained fluid when one of the cysts becomes very large and symptomatic. Deroofing the exposed portion of the cyst, if the contents are clear and uninfected and internal enteric drainage of bile-containing or infected cysts are the procedures of choice.

The *solitary congenital* cysts are the second most common (2). These lesions have been reported to be more frequent in women, on a 4:1 ratio (3). Liver function tests are normal in most patients and usually the only symptoms are caused by the enlargement of the liver cyst (7).

The treatment can be total excision, if the cyst is small and superficial. When the contents of the cyst are clear without any evidence of bile or infection, deroofing the cyst, and either leaving it in free communication with the peritoneal cavity or using a pedicle of omentum to pack the dead space, is the acceptable management (12). The possibility of a communication of the cyst with the biliary system should be excluded by an intra-operative cholangiogram (13), for if such is present, then an internal drainage procedure



should be performed. The procedure of choice for internal drainage, when bile is present in the cyst, is an anastomosis of its most dependent part, to a Roux-en-Y jejunal limb. When infection and purulent material are present, the cyst should be drained or marsupialized until the infection is controlled.

The *traumatic* cysts arise from contusion of the deeper-lying tissue with preservation of the overlying hepatic capsule. They are devoid of epithelial lining and contain a mixture of blood, bile and degenerated liver tissue. It is thought that even after the initial bleeding stops, the flow of bile continues and gradually the cavity enlarges producing symptoms after a considerable interval of time subsequent to the injury (9).

Management follows the same guidelines as in solitary cyst.

*Inflammatory* cysts are the pyogenic liver abscesses and they will not be discussed in this paper.

Finally the *neoplastic* cysts are typically lined by a proliferative epithelium that exhibits papillary extensions projecting into the cavity of the cyst. The benign variety is the cystadenoma and the malignant counterpart, the cystadenocarcinoma. Both types are very rare. In the neoplastic varieties, any surgical procedure short of complete excision is likely to be followed by recurrence (10). Usually a lobectomy is the procedure of choice (11).

### Conclusion

The surgical management of hepatic cysts is marked by several problems, specially recurrences. A simple systematic approach to establishing a diagnosis before surgery as well as accurate determination of possible communications between the biliary system and the cyst, help to make the choice of surgical procedure for the patient.

Attention to technique and choosing the surgical procedure indicated for the particular type of cyst should prevent some of these complications.

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## PSIQUIATRIA: 1979

Néctar de la R. de Torregrosa, MD

La enseñanza y la práctica de la Psiquiatría ha cambiado mucho en los últimos años. Este artículo va dirigido al médico moderno que interesa conocer sobre la posición actual de la Psiquiatría en la Medicina. Es necesario señalar que la presentación es limitada en cuanto a punto de partida y a referencias de personas y sucesos que facilitaron los cambios, dada la magnitud infinita de estos. Se acompaña una bibliografía que puede ayudar al lector interesado a ampliar su visión del mundo actual de la Psiquiatría.

La década del cincuenta marcó la entrada de Psiquiatría como disciplina a enseñarse en Medicina (1). Para 1956 el Comité de Educación Médica de la Asociación Americana de Psiquiatría produjo el bosquejo donde se especificaban los requisitos mínimos en la enseñanza de Psiquiatría en currículos de escuelas de Medicina (1). Para esa época, en Puerto Rico la enseñanza de psiquiatría a estudiantes de Medicina se ofrecía dentro de Medicina Interna como una sub-especialidad. Para 1957-58 este adiestramiento cobró fuerzas: se estableció el Departamento de Psiquiatría de la Escuela de Medicina dirigido por el doctor Juan A. Roselló y se comenzó a enseñar Psiquiatría como una de las disciplinas principales\* en el currículo. Esa fecha también marcó el inicio de preparar al primer grupo de psiquiatras que egresaría de nuestra Escuela. El doctor Juan E. Morales era el director del Programa de residencia.

Para esa época, veinticinco años atrás, el id. ego, superego y la personalidad, el inconsciente, preconsciente y consciente eran el estetoscopio del psiquiatra. Esto, dada la influencia del doctor S. Freud quien, a fines

del siglo pasado y principios de éste, describió la estructura interna psicológica del ser humano (personalidad), elaboró una teoría de desarrollo de esta estructura (teoría psicosexual) y una técnica para investigarla (el psicoanálisis) (2).

Cierto es que algunos discípulos (Jung, Adler, Rank) contrariados con las teorías del maestro, al igual que otras personas ajenas a él (Piaget, Pavlov, Gesell) buscaron para ese tiempo otros cómo y por qué de la conducta humana. También es cierto que la teoría de la libido y catexis, los instintos y el predeterminismo, prevaleció en la formación y ejecutorias del psiquiatra durante la primera mitad de este siglo. Sin embargo, esto no desanimó a los contrarios ni a sus seguidores a continuar buscando otras explicaciones (3, 4, 5, 6).

Tal fue así que, para la década del cuarenta, este insumo se dió a notar resultando en una revisión y ampliación de la teoría original por parte de aquellos que la seguían y practicaban. En ese movimiento de revisión también influyó los efectos de la segunda guerra mundial en el comportamiento de algunas poblaciones, en particular los huérfanos de guerra, los prisioneros de guerra y los ex-combatientes (6, 7, 8).

Algunos freudianos focalizaron en diferentes aspectos de la teoría. Unos (H. Hartman, E. Kris, R. M. Lowenstein, R. Spitz, M. S. Mahler) estudiaron el ego: su estructura, funciones y desarrollo mientras que otros (W. Reich, H. Nagera, I. Steingart, P. Blas, A. Peto, L. A. Spiegel, J. Lamp-de-grot), hicieron lo mismo con otras estructuras de la personalidad. Se estudió y se elaboró sobre los fenómenos afectivos que se dan en las relaciones interper-

sonales (E. Jacobson, G. L. Bibring, J. Bowlby, H. Stack Sullivan, R. Spitz, N. W. Ackerman); sobre los fenómenos perceptivos en los primeros años de vida (S. K. Escalona, R. Spitz); sobre la relevancia que la sociedad/cultura tienen en el desarrollo de la persona (E. Erikson). Este movimiento aún persiste y ha dado lugar a una expansión y enriquecimiento de las técnicas psicoterapéuticas. Las tendencias del movimiento apuntaron a estudiar la persona a través tanto de su mundo interno psicológico como del externo (ambiente que la rodea) (3, 4, 7, 9, 10, 11, 12, 13).

Para fines de la década del cincuenta, la introducción al mercado de los psicofármacos, reabrió las puertas del componente biológico (14). Este último estaba casi en desuso como área de intervención ya que se temía por las repercusiones adversas que las alternativas disponibles (choque insulínico, electrochoque, psicocirugía, etc.) pudieran tener en la persona en el futuro. El uso de neurolépticos facilitó que se desarrollaran técnicas más precisas para estudiar las bases biológicas del comportamiento humano (14). Durante los últimos veinte años se han hecho grandes adelantos en la bioquímica de los neurotransmisores (J. Axelrod, B. B. Brodie, E. Costa, S. H. Snyder, A. B. Young), en la neurofisiología del sueño (E. Aserinsky, W. C. Dement, E. Hartman, A. Kales, N. Kleitman), en estudios de ritmos biológicos (P. Wolff, S. Stroevel), de stress (H. Selye, B. Wolf, H. Wolff); en la neuroanatomía (J. Papez, W. Penfield, P. Maclean, Luria) y en el impacto de los factores genéticos (F. J. Kallmann, J. D. Rainer, D. Rosenthal), todos estos relacionados a la conducta humana. Se comenzó entonces a hablar de Medicina Psicosomática (F. Alexander, T. French, T. Benedeck) (6).

Concurrente al insumo sicoanalítico y biológico, las disciplinas que estudian las interacciones entre personas, la dinámica social, la formación de grupos, la evolución de patrones de comportamiento, el establecimiento

de roles, valores esterotipos en sociedades y culturas dadas, también contribuyeron a expandir el campo de la Psiquiatría. A esto aportaron, entre otros, los estudios ecológicos de Lorenz y Harlow, la psicología experimental (W. H. Gantt, H. Liddell, S. K. Escalona, L. R. Fantz, H. G. Furth) la antropología (M. Mead, R. Benedict) y los trabajos con grupos (G. Bateson, V. Satir, D. Jackson, J. Haley, T. Lidz, J. Moreno, S. R. Slavson, K. Lewin, A. Hollingshead). Todas estas aportaciones se hicieron cada vez más evidentes a partir de la década del cincuenta (6).

Para la década del sesenta, sostenida en los Estados Unidos por el Servicio Público de Salud (Instituto Nacional de Salud Mental, fundado en 1949) y por la aceptación de la población en general, la Psiquiatría ya existía como disciplina con particularidad propia en cuanto a marcos teóricos, enfoques terapéuticos y niveles de intervención dentro de la Medicina (15). Simultáneamente, la guerra de Vietnam, las manifestaciones de violencia en varios lugares, los confrontamientos raciales, el abuso de drogas, las manifestaciones de liberación por parte de varios grupos, impactó la Psiquiatría (6). La tendencia general resultante fue la de incorporar la identificación y solución de problemas sociales como contenido importante en la preparación del psiquiatra (1, 6, 13, 15).

Así pues, al comenzar la década del setenta, el campo de la Psiquiatría se había expandido para incluir el estudio e intervención en poblaciones de todas las edades a nivel de una persona, grupos pequeños o comunidades; con una gama de alternativas terapéuticas que van de labiocelular, a lo psicosocial, a lo social hasta lo ético. Esto se demuestra en las diferentes modalidades que hoy día existen en la práctica de la Psiquiatría: Psiquiatría clínica general, de Niños y Adolescentes, Forense, de Familia, de Comunidad, de Enlace (liaison) y Biopsiquiatría. Cada una de estas tiene particularidades en cuanto a la población



que sirve, sus marcos conceptuales y alternativas de diagnóstico y tratamiento. Hoy, 1979, en Puerto Rico, la preparación de un psiquiatra requiere que adquiera conocimiento y desenvolvimiento práctico en todas y cada uno de esos modelos.

En términos generales se espera que el psiquiatra moderno pueda:

1. utilizar adecuadamente su sí mismo instrumento evaluador, terapéutico y facilitador de conducta humana.
2. utilizar al óptimo los varios recursos (biológicos, físicos, sociales, y humanos) en el proceso de dar y recibir ayuda.
3. llevar a cabo intervenciones a niveles primarios, secundarios y terciarios con poblaciones de varias edades y según sea necesario.
4. llevar a cabo tareas de consultoría, enlace, educación, administración, en diferentes áreas de práctica, (hospital, clínicas externas, escuelas, cortes y comunidad en general) según sea el caso.
5. utilizar nuevas técnicas en la investigación científica de las enfermedades mentales.
6. mantenerse al día en su profesión y en lo que ocurre a su alrededor en lo que concierne a la Salud Mental.

Sobre esto último, como ya habrá notado el lector, el campo de la Psiquiatría (al igual que el resto de la Medicina) está en constante cambio y desarrollo. Cada puerta que se abre deja ver que al fondo hay muchas más por abrir. Actualmente, por ejemplo, la interven-

ción del psiquiatra con la población de ancianos, en las áreas de Política Pública, Pedagogía, Administración e Investigación, está en sus inicios. Trabajar cada una de estas resulta descubrir más avenidas donde el psiquiatra es necesitado y puede contribuir dado su preparación.

Hoy, 1979, al igual que a principios del siglo, la Psiquiatría sigue siendo la rama de la Medicina que se dedica a evaluar e intervenir con cambios en el comportamiento de las personas en lo referente a estados de salud-enfermedad. Difiere de la Psiquiatría de la primera mitad del siglo en que la población que puede ser atendida se ha expandido a incluir las varias edades, grupos pequeños, familias, y comunidades; en que se brega en los tres niveles de prevención y en que se conceptualiza simultáneamente en formas analítica (particularizar) e integral (generalizar).

Hoy día (aunque suene paradójico) además de ser una especialidad en la Medicina, la Psiquiatría, junto a las ciencias biomédicas, es base para el estudio de la Medicina. Por un lado, los instrumentos y conceptos de la Psiquiatría son base para poder bregar efectivamente con las personas, y esto es buena medicina moderna. Por otro lado, parte de la Psiquiatría es diagnosticar y atender personas que demuestran disturbios en su comportamiento y en ese sentido es una especialidad de la Medicina.

La atención adecuada al ser humano en sus estados de salud-enfermedad es la razón de ser de la Medicina. Practicarla sin conocer Psiquiatría es curar un hígado, eliminar unas bacterias o tratar síntomas/signos sin haber realmente atendido a la persona, a la familia o a la comunidad en sus manifestaciones de Salud-Enfermedad.

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## LISTA DE ANUNCIANTES

BURROUGHS WELLCOME  
Neosporin  
Septra

MEAD JOHNSON  
Duricef

PFIZER  
Sustaire

ROCHE LAB  
Librium  
Valium

RORER INTERNATIONAL  
Maalox Plus

SMITH KLINE DIAGNOSTICS  
Isocult

SMITH, KLINE & FRENCH  
Tagamet

U.S.V. PHARM.  
Hygroton 25

## TUBERCULOSIS: CONCEPTOS ACTUALES - PARTE II

Ramón Ramírez Ronda, MD y Carlos H. Ramírez Ronda, MD, FACP

### Quimioterapia

La quimioterapia está en un estado de cambio y podemos dividirla entre lo que consideramos quimioterapia clásica, quimioterapia bifásica, quimioterapia intermitente y quimioterapia de corta duración.

### Quimioterapia Clásica

Se ha demostrado que hay resistencia natural a isoniácida en alrededor de uno de cada 100,000 microorganismos y que la resistencia primaria a la estreptomycin es de 1 en 1,000,000. El tratamiento con dos drogas, a las cuales el microorganismo es susceptible, evita el surgimiento de cepas resistentes. La incidencia de resistencia primaria en los E.U.A. se ha rastreado constantemente en los últimos quince años. Los resultados indican que el 93 por ciento de las cepas aisladas, son susceptibles a las cuatro drogas de primera línea, y que la resistencia primaria no está aumentando (49). Los datos para Puerto Rico sobre resistencia a drogas antituberculosas provienen de un estudio de 45 cultivos, demostrando

sobre 90 por ciento de resistencia. El 22 por ciento de resistencia primaria se registraba cuando se incluían todos los medicamentos incluyendo la cicloserina (50). La resistencia primaria a isoniácida se mantiene aproximadamente en un 0.8 por ciento en los E.U.A. No tenemos datos recientes y específicos para Puerto Rico. Debido a esta baja incidencia de resistencia primaria en el tratamiento diario con cualquiera de las dos drogas de primera línea debe predecirse efectividad en exceso del 95 por ciento. Numerosos estudios han confirmado esta observación, y los resultados varían solamente en la tasa de esterilización del esputo. Usualmente, esta no puede correlacionarse con una mejoría clínica (43, 51, 52, 53). La selección de drogas en esta situación se basa en cuán fácil es la aceptación del paciente, los efectos secundarios y costos. En las tablas I y II presentamos las drogas anti-tuberculosas de primera y segunda línea incluyendo dosificación, efectos secundarios y los parámetros que deben de seguirse cuando se administran estas drogas (54).

La isoniácida combina una gran efectividad con una toxicidad y con un costo muy bajos. Esta resulta ser el agente principal en el tratamiento de tuberculosis. Se absorbe bien y es bactericida en contra de los organismos que se están multiplicando. Reacciones de hipersensitividad, resultando en hepatitis clínica, o aún en hepatitis fulminante, ocurren en aproximadamente 1 por ciento de los que la reciben. Elevaciones de transaminasa pueden esperarse en 10 por ciento de los pacientes, y puede requerir que se descontinúe el tratamiento en algunos casos (55). En las personas que son inactivadores lentos de isoniácida, no se ha

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TABLA I

Tratamiento de Enfermedad Mycobacteriana  
Drogas de Primera Línea

DROGA	DOSIS DIARIA	DOSIS DOS VECES POR SEMANA	EFFECTOS SECUNDARIOS	SEGUIMIENTO
ISONIACIDA	5-10 MG/KG HASTA 300 MG PO O IM	15 MG/KG PO O IM	NEURITIS PERIFERICA, HEPATITIS HIPERSENSITIVIDAD	SGOT/SGPT
ETAMBUTOL	15 MG/KG PO	50 MG/KG PO	NEURITIS OPTICA, ERUPCION EN PIEL	DISCRIMINACION ROJO-VERDE AGUDEZA VISUAL
RIFAMPIN	10-20 MG/KG PO HASTA 600 MG	----	HEPATITIS, FIEBRE, PURPURA	SGOT/SGPT
ESTREPTOMICINA	15-20 MG/KG HASTA 1 GM IM	25-30 MG/KG IM	DAÑO 8VO NERVIO NEFROTOXICIDAD	FUNCION VESTIBULAR

PO - Por boca

IM - Intramuscular

correlacionado este hecho con toxicidad hepática o respuesta a tratamiento en la dosis usual de 5 a 10 mg/kg (56). Se sabe que la neuritis periférica ocurre en más del 50 por ciento de los activadores lentos si la dosificación de isoniácida se aumenta a 15 mg/kg. El suplemento con piridoxina es usualmente innecesario a menos que se sospeche deficiencia de piridoxina o que se considere utilizar dosis altas de isoniácida (57). En pacientes que requieren difenylhidantoina (Dilantin) y que están utilizando isoniácida, la dosificación de difenylhidantoina debe ser reducida a 100 - 200 mg diariamente para prevenir los efectos secundarios en el sis-

tema nervioso central (58).

Etambutol es la droga que se utiliza en la actualidad como compañera de isoniácida en el tratamiento diario de tuberculosis. Es una droga bacteriostática que cuando se combina con isoniácida convertirá el esputo del paciente a negativo con seis meses de tratamiento en más del 97 por ciento de los casos. El único efecto secundario importante está relacionado con la dosificación y es neuritis óptica. Esta toxicidad ocurre en aproximadamente 3 por ciento de aquellos pacientes que se le administran 25 mg/kg, pero es rara en la dosis usual de 15 mg/kg (59). Debido a que etam-

TABLA II

Tratamiento de Enfermedad Mycobacteriana en  
Drogas de Segunda Línea

DROGA	DOSIS DIARIA	EFFECTOS SECUNDARIOS	SEGUIMIENTO
VIOMICINA	15-30 MG/KG HASTA 1 GM IM	DAÑO 8VO NERVIO, NEFROTOXICIDAD, TOXICIDAD VESTIBULAR	FUNCION VESTIBULAR, AUDIOGRAMA, BUN, CREAT.
CAPREOMYCINA	15-30 MG/KG HASTA 1 GM IM	DAÑO 8VO NERVIO, NEFROTOXICIDAD	LO MISMO
KANAMYCINA	15-30 MG/KG HASTA 1 GM IM	DAÑO 8VO NERVIO, NEFROTOXICIDAD, TOX, VESTIBULAR	LO MISMO
ETIONAMIDA	15-30 MG/KG HASTA 1 GM PO	GI, HIPERSENSITIVIDAD, HEPATOXICIDAD	SGOT/SGPT
PYRAZINAMIDA	15-30 MG/KG HASTA 2 GM PO	HIPERURICEMIA, HEPATOTOXICIDAD	SGOT/SGPT ACIDO URICO
ACIDO PARAAMINO SALICILICO	150 MG/KG HASTA 12 GMS PO	GI, HIPERSENSITIVIDAD HEPATOTOXICIDAD HIPERNATREMIA	SGOT/SGPT
CYCLOSERINA	10-20 MG/KG HASTA 1 GM PO	PSICOSIS, CAMBIOS PERSONALIDAD, CONVULSIONES ERUPCION	PRUEBAS PSICOLOGICAS

butol se excreta en la orina, su dosificación debe reducirse en fallo renal.

Rifampin, al igual que la isoniacida, es bactericida y extremadamente efectivo en el tratamiento de tuberculosis. Se excreta a través del sistema biliar y los riñones. Es el agente más efectivo produciendo conversión de esputos aun más rápido que cual-

quier otra combinación que se utilice. A pesar de que la tasa de recaída es pequeña, la incidencia de hepatotoxicidad es alrededor de 8 por ciento en aquellos pacientes que se le administra la combinación isoniacida-rifampin (51). La toxicidad hepática aumenta en la presencia de enfermedad hepática previa (60). Otros efectos secundarios incluyen reacciones

de hipersensitividad, trombocitopenia, leucopenia y depresión de la respuesta inmune. Estas reacciones han ocurrido mayormente cuando rifampin se ha administrado intermitentemente y está contraindicado utilizar rifampin en cursos de tratamiento intermitente.

La estreptomicina, cuyo uso está limitado a la administración parenteral, la cubriremos en el regimen de tratamiento intermitente de dos fases. Su toxicidad hacia el octavo par craneano, así como su toxicidad renal, son bien conocidas y usualmente reversibles.

Las drogas de segunda línea son útiles solamente cuando ha ocurrido recaída con organismos resistentes a las drogas primarias. Esta situación usualmente se encuentra solamente en pacientes que prematuramente descontinúan su tratamiento inicial. El concepto de añadir dos drogas nuevas a las cuales el organismo es susceptible ha resultado en una efectividad mayor de 90 por ciento cuando el tratamiento ha sido supervisado de cerca (48).

Las recomendaciones para la duración de tratamiento con dos drogas en pacientes con enfermedad moderada a avanzada es de 18 a 24 meses. Esta recomendación está basada en una tasa de recaída de 18 por ciento en aquellos pacientes tratados por doce meses versus solamente dos por ciento en aquellos tratados 24 meses (61).

### Quimioterapia Bifásica e Intermitente

A pesar de que la quimioterapia diaria ha probado su efectividad, la incidencia de fracasos en terapia primaria a los seis meses es significativa (61). Estos fracasos se deben a que algunos pacientes no siguen las instrucciones durante su tratamiento ambulatorio (62-64). La quimioterapia de corta duración supervisada, esto es seis meses, da apoyo a la idea que la mayor parte de los fallos en el tratamiento primario son secundarios a que

el paciente no siga las instrucciones.

Debido a la importancia de este problema, particularmente en las poblaciones de alcohólicos, se ha investigado los regímenes terapéuticos bifásicos intermitentes. Estos están basados en el conocimiento de la acción específica de las drogas y en el estimado de la población bacilar total (65).

La población de bacilos en una lesión tuberculosa se ha demostrado que varía con la morfología de ésta. Canetti ha demostrado que de  $10^2$  a  $10^5$  microorganismos pueden estar presentes en lesiones pulmonares nodulares, mientras que en las lesiones cavitarias la población puede llegar hasta  $10^{11}$  (66). Aún más, en las lesiones cavitarias los bacilos de tuberculosis se multiplican mucho más ligero que en lesiones cerradas. Por lo tanto, el éxito del uso de isoniacida sola, en los casos de tuberculosis primaria puede deberse a las poblaciones de bacilos pequeñas y es un reflejo del número pequeño de organismos resistentes a drogas que ocurren (67).

Isoniacida y Rifampin son ambos bactericidas y más activos en contra de los microorganismos que se están dividiendo rápidamente; también son efectivos en contra de los microorganismos intracelulares y microorganismos atenuados. Ambos cruzan fácilmente las membranas biológicas incluyendo la barrera hematocefálica. Las concentraciones de estos dos agentes dentro de las lesiones tuberculosas se aproximan a las concentraciones que se encuentran en la sangre (68, 69, 70). La estreptomicina es solamente bactericida a un pH alcalino y más efectiva en contra de microorganismos extracelulares (71, 72). Se ha demostrado sinergismo bactericida entre isoniacida y estreptomicina (79). Etambutol es bacteriostático y probablemente más activo en contra de microorganismos intracelulares o microorganismos atenuados (74).

El tamaño de la población bacilar y las propiedades de las drogas individuales han resultado en el concepto de que la quimio-



terapia en dos fases puede llevarse a cabo. Esto es, un período inicial con quimioterapia intensiva cuando la población bacilar es grande, extracelular y dividiéndose rápidamente; seguida por un curso menos intensivo cuando los organismos han sido substancialmente reducidos. Este concepto es aplicable solamente en pacientes que tengan evidencia radiológica de enfermedad avanzada, donde la población bacilar se puede demostrar que sea grande. Estudios clínicos han demostrado la validez de este concepto demostrando que ocurre una conversión de esputo más rápidamente cuando la estreptomycin se añade por un corto tiempo a varios regímenes de dos drogas (53, 75).

Después que disminuya la población bacteriana, el uso de un regimen de dos drogas diariamente por un período de 18 a 24 meses resulta en un éxito que se aproxima a un 99 por ciento cuando el paciente lleva a cabo el tratamiento (46, 76).

Aún con el regimen bifásico se encuentran fracasos debido a que los pacientes discontinúan sus medicinas durante la fase menos intensiva de tratamiento (77, 78). Desde los años 50 se pensó que un regimen bisemanal intermitente de quimioterapia recibiría una aceptación más grande por los pacientes. La efectividad de la administración intermitente de drogas fue investigada primeramente por el Centro de Tuberculosis en Madras, India. Ellos evaluaron el uso de isoniácida 14 mg/kg y estreptomycin 27 mg/kg administrado dos veces semanalmente por un año y compararon esto con isoniácida más ácido paraminosalicílico administrado diariamente por el mismo período. Los resultados de esta prueba demostraron lo siguiente (79); de los pacientes que recibieron el regimen de isoniácida y ácido paraminosalicílico diariamente, el 85 por ciento estaba bacteriológicamente negativo a los doce meses, y el 15 por ciento restante tuvo una recaída en cuatro años; mientras que del grupo que recibió isoniácida más estreptomycin dos veces

en semana, el 94 por ciento estuvo bacteriológicamente negativo a los doce meses, y la recaída a cuatro años fue del 12 por ciento. Habiéndose demostrado la eficacia clínica, Dickinson y colaboradores diseñaron estudios para predecir cuales drogas debían ser más efectivas en un regimen de quimioterapia intermitente (80). Como es de esperarse, las drogas más efectivas serán aquellas que sean bactericidas y que tengan la habilidad de inhibir el crecimiento de los organismos por un tiempo prolongado después de haber tenido una exposición al medicamento por un tiempo corto. Los resultados indican que estreptomycin es altamente efectiva y que isoniácida es algo menos efectiva en tratamiento intermitente. Trabajos más recientes han indicado que rifampin, etambutol y pirazinamida son también efectivos (81-83).

Cuando los regímenes intermitentes fueron probados en modelos experimentales de tuberculosis en ratones, los resultados de tratamiento después de tres meses con isoniácida y estreptomycin dos veces en semana no fueron tan buenos como el resultado de tratamiento diario con las mismas drogas (84). Con el mismo modelo experimental en el ratón, un período inicial corto, de tratamiento diario, produce considerablemente mejores resultados. Con dosis más bajas de las drogas por un período más largo de tratamiento, 3 meses, seguido por tratamiento intermitente los resultados fueron tan buenos como el uso de tratamiento diario continuo (85).

Los resultados utilizando el modelo de animales ha estimulado a muchos investigadores a combinar el tratamiento inicial intensivo con el tratamiento intermitente. En la mayor parte de las investigaciones, el tratamiento intermitente que sigue ha sido efectivo tanto en la conversión de esputo como en la prevención de recaídas (86, 87). Si se utiliza isoniácida, estreptomycin y ácido paraminosalicílico diariamente por tres meses y luego

se cambia a tratamiento intermitente de isoniácida más estreptomina dos veces en semana por 18 meses, y se compara con un tratamiento continuo de isoniácida y estreptomina, los resultados del regimen continuo versus el regimen intermitente son como sigue: a los 18 meses de tratamiento el 100 por ciento de los pacientes que han recibido el tratamiento continuo está bacteriológicamente negativo al igual que el 99 por ciento de los que recibieron el tratamiento bifásico intermitente. El número de recaídas a 36 meses fue cero en ambos grupos, demostrando la efectividad.

En contraste con los datos en animales, las pruebas clínicas por el grupo de Madras, nuevamente demostraron que isoniácida más estreptomina administrado dos veces en semana en el comienzo de tratamiento fue extremadamente efectivo. Pero en el mismo estudio, isoniácida más estreptomina administrado solamente una vez por semana fue inefectivo (88).

Se ha demostrado que los regímenes de dos veces por semana de isoniácida y estreptomina o isoniácida y etambutol son efectivos como regímenes de continuación de tratamiento. Rifampin no se recomienda en ningún regimen intermitente, ya que su toxicidad aumenta cuando se administra de esta manera (89).

Basándose en estos estudios y en otros estudios en poblaciones de pacientes más grandes se puede deducir que la administración de quimioterapia intermitente supervisada es efectiva en el tratamiento inicial de tuberculosis en países en desarrollo. En los Estados Unidos de Norte América se ha demostrado que el tratamiento supervisado por largo tiempo es inefectivo debido a problemas y limitaciones de organización. En países donde las limitaciones son mayores, una fase intensiva inicial de tratamiento seguida por un regimen dos veces en semana parece ser más efectiva, específicamente para aquellos pacientes recalcitrantes que rechazan tratamiento. Si un regimen similar debe

adoptarse en Puerto Rico, deben requerirse estudios controlados.

### Quimioterapia de Corta Duración

El éxito clínico de los regímenes intermitentes y la demostración de que el uso de drogas bactericidas son efectivas, ha estimulado la investigación de los regímenes de terapia de duración corta (90-92). Estas investigaciones fueron iniciadas en los países en desarrollo donde los recursos financieros son mínimos, y el tratamiento de 18 meses de duración supervisado directamente no es posible debido a problemas organizacionales. Los resultados tienen implicaciones a largo plazo para el tratamiento de tuberculosis aún en los países más desarrollados. Las ventajas son: una cantidad total menor de drogas administradas y por lo tanto una esperanza en mejorar el cumplimiento de los pacientes con su tratamiento.

El primero estudio fue conducido en África del Este. Las drogas fueron administradas diariamente por un total de seis meses y estudios subsiguientes en el momento han dado seguimiento a los pacientes hasta por 48 meses (93). El regimen de isoniácida, estreptomina y rifampin con el cual se trataron 152 pacientes tuvo una recidiva de 8 por ciento y el regimen de estreptomina e isoniácida con el cual se trataron 112 pacientes tuvo una recidiva de 29 por ciento, demostrando así la efectividad y superioridad del regimen corto de isoniácida, estreptomina y rifampin en este grupo de pacientes.

Se concluyó de este estudio que dos de las combinaciones de tres drogas producían un porcentaje de recidivas bacteriológicas aceptables y aún más se demostró que en aquellos que ocurrió recaída, los microorganismos eran susceptibles a las drogas administradas (94, 95).

Un segundo estudio hecho en África del Este confirmó las observaciones iniciales



y los resultados a 30 meses de seguimiento son como siguen: el regimen de isoniacida, estreptomycin y rifampin por seis meses resultó en un 2 por ciento de recidiva a 30 meses mientras que el regimen de isoniacida y rifampin resultó en 7 por ciento de recidiva a 30 meses. A pesar de que el regimen de dos drogas de isoniacida y rifampin tuvo un índice de recidiva aceptable, el añadir la estreptomycin hizo una diferencia pequeña pero estadísticamente significativa confirmando nuevamente la importancia de una terapia inicial intensa (96, 97). Estos estudios fueron conducidos en países donde la tasa inicial de resistencia es mucho más alta que en los Estados Unidos de Norte América.

Varios investigadores han debatido el valor de las pruebas de susceptibilidades iniciales *in vitro* para *M. tuberculosis*, aunque sostienen que estas pruebas añaden muy poco al manejo de pacientes (98). Los estudios de Africa del Este y subsiguientemente los estudios de Hong Kong dan evidencia sobre este concepto. En ambos estudios la respuesta clínica no correlacionó necesariamente con las pruebas de susceptibilidad de *M. tuberculosis*, el índice de recidivas fue pequeño y usualmente ocurrió con organismos susceptibles a drogas (99, 100). Si se eliminan las pruebas de susceptibilidad en un segundo tratamiento de rutina en la población de los E.U.A., la cual tiene individuos susceptibles a las drogas primarias, debiera esperarse un éxito inicial alto. En esta situación un segundo tratamiento con un regimen de reserva, se utilizaría solamente en los pacientes que permanecen bacteriológicamente positivos después de 6 meses de tratamiento (98, 99). Estos datos también tiene implicaciones para la reinstitución de quimioterapia en los pacientes que no siguen el regimen prescrito. Si el tratamiento ha sido iniciado con dos o tres drogas de primera línea y todas las drogas fueron terminadas simultáneamente, la reinstitución de las mismas drogas debe ser la apropiada; ya que las recidivas son mayormente

con organismos susceptibles a estas drogas. Este concepto no aplica cuando solamente una droga fue descontinuada del tratamiento, ya que la resistencia a este medicamento puede entonces ser estadísticamente posible.

La quimioterapia de corta duración en los países en desarrollo está todavía en una etapa investigativa; más en el futuro el uso en el paciente que no sigue instrucciones médicas es realista. Con un regimen supervisado ambulatorio diario de seis meses debe esperarse eliminar el problema de reactivación de tuberculosis, ya que los pacientes serían todos tratados y el índice de recidivas es bien bajo.

### Infectividad, Hospitalización y Altas de la Clínica

#### *Infectividad:*

En 1934 H. G. Wells demostró que la infección por tuberculosis era producida por pequeños núcleos de secreciones que más tarde demostraron ser de menos de 10 micras en diámetro (101). Las partículas más grandes se depositaban en el tracto respiratorio alto y no producían infección, por lo tanto para que ocurriese infección las partículas debían de deshidratarse antes de que ocurriese diseminación aérea (102). Ya para 1947 se demostró que los ropajes usados en el hospital y de los pacientes no eran importantes en la transmisión de infección tuberculosa (103). Se demostró también que si las partículas pequeñas eran expuestas a luz ultravioleta esto evitaba la infección en animales experimentales (104). El número de pequeñas partículas en una manipulación expiratoria depende de la velocidad del aire expirado (105). Por lo tanto, el toser y el estornudar son los diseminadores importantes de infección. Si la boca y la nariz se cubren, se disminuye grandemente el riesgo de infección. Una vez comienza la quimioterapia, se ha demostrado que el paciente tose menos



aún con la primera semana de tratamiento (106).

En 1960 Sultan y colaboradores encontraron que las concentraciones de isoniácida en el esputo se aproximaban a aquellas de la sangre (107); por lo tanto, según la gota se evapora y se disminuye en volumen, la concentración debe de aumentar miles de veces.

Aún más, evidencia indirecta del potente efecto esterilizante de la isoniácida fue demostrado primeramente por Reilly y asociados. En su modelo experimental expuso coballos al aire exhalado de pacientes con esputos positivos antes de comenzar el tratamiento. El estudio tuvo una duración de 2 años y envolvió la exposición continua de 175 coballos. Durante los dos años, solamente 71 animales se infectaron; y solo dos de ellos con cepas resistentes a drogas. Durante el período de cuatro meses, cuando todos los pacientes con esputo positivo tenían organismos susceptibles a drogas, ninguno de los animales se infectó (108).

#### *Hospitalización:*

El primer estudio que documenta el efecto potente de drogas en revertir infección en una población humana fue conducido en Madras, India en 1966. Comparando números grandes de pacientes tratados exclusivamente en la casa o en el sanatorio, la infección tuberculosa se desarrolló en 9.4 por ciento de los contactos del grupo que fue tratado en la casa y en el 14 por ciento de los que fueron tratados en el sanatorio (109). Este trabajo ha sido confirmado por otros estudios conducidos en los E.U.A. y los resultados de estos estudios son como siguen: un grupo con esputo positivo tenía estos positivos después de un mes de tratamiento y fue enviado a su casa a continuarlo. El segundo grupo con esputos positivos fue tratado en el hospital hasta que los esputos se convirtieron en negativos. En los pacientes con esputos positivos, el 40 por

ciento de los contactos, y el 42 por ciento de los contactos menores de 16 años reaccionaron a la tuberculina, mientras en los contactos de grupos con esputos negativos fue un 38 por ciento. No se demostró diferencia entre los grupos en reactividad a tuberculina en contactos dentro de la casa incluyendo niños. Estudios subsiguientes han disminuído la hospitalización a dos semanas, y nuevamente demostraron que no ha aumentado la reactividad a tuberculina en contactos en las casas (111).

Todos estos datos dan apoyo a las recomendaciones recientes que *la hospitalización de pacientes con tuberculosis pulmonar depende de su condición médica en general*. El momento preciso en donde ellos se convierten en no infecciosos está relacionado con la susceptibilidad a las drogas del microorganismo, pero probablemente ocurre cerca o inmediatamente después de instituir el tratamiento.

La respuesta clínica a quimioterapia ocurre frecuentemente en la primera semana, los pacientes demuestran disminución en tos y producción de esputo (106). Si se requiere la hospitalización, la decisión de dar de alta debe estar basada en la respuesta clínica en total del paciente y debe de correlacionarse con el estado nutricional del paciente. La presencia de microorganismos en el frotis de esputo no correlaciona con infectividad una vez se ha iniciado el tratamiento adecuado.

#### *Alta de la Clínica:*

El éxito del control moderno de tuberculosis depende de la facilidad de tener unos buenos programas ambulatorios para el tratamiento de estos pacientes (112). Las clínicas ambulatorias deben de estar capacitadas para proveer cuidado rutinario y para bregar con los pacientes que no siguen las instrucciones; proveyendo tratamiento supervisado cuando es necesario. Si este servicio se provee y un curso de quimioterapia adecuada

se completa, la posibilidad de reactivación durante la vida de este paciente será solamente de alrededor de 0.8 por ciento (113, 114).

Debido a que los programas de rastreo continuo tienen una productividad muy baja, esto ha resultado en que se recomiende que aquellos pacientes en donde se conoce que han completado un curso de quimioterapia se consideren curados. Entonces estos pacientes son dados de alta de exámenes de rutina pero se les da instrucciones para que vuelvan a la clínica si los síntomas se desarrollan nuevamente (115).

En este repaso sobre la quimioterapia de tuberculosis en 1979 hemos presentado la magnitud y el espectro del problema. Hemos tratado de presentar la patogénesis, espectro clínico y la respuesta inmunológica de la tuberculosis pulmonar primaria y de la tuberculosis pulmonar crónica. Hemos establecido lo que consideramos las reglas para el diagnóstico de tuberculosis en la actualidad y hemos tratado de dirigir e ilustrar la quimioterapia de la tuberculosis pulmonar basándonos en la clasificación por grupos y comparando los regímenes de la quimioterapia clásica, la quimioterapia bifásica e intermitente y la quimioterapia de corta duración. Esperamos que con este repaso podamos ayudar a actualizar los conceptos del manejo de tuberculosis en el Puerto Rico de hoy.

Recomendamos que en el momento se continúe el manejo de tuberculosis en Puerto Rico por el régimen de quimioterapia clásica. Sugerimos que se considere estudiar bajo condiciones controladas los regímenes alternos para ver su posible aplicación dentro de nuestra idiosincrasia de pueblo.

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### CONTESTACIONES A MEDI-QUIZ

1. b, c
2. b, d
3. d
4. d
5. d
6. b
7. a
8. a
9. c
10. c

DISCURSO PRONUNCIADO POR EL DR. GERARDO SANZ ORTEGA  
AL TOMAR POSESION COMO PRESIDENTE DE LA ASOCIACION  
MEDICA DE PUERTO RICO EL 10 DE NOVIEMBRE DE 1979

Constituye para mí un honor y un privilegio el dirigirme a ustedes por primera vez como Presidente de esta prestigiosa Asociación Médica de Puerto Rico, quien reúne en su seno al mayor número de galenos dentro de la medicina organizada, y que desde su fundación por el Dr. Quevedo Báez en 1902, ha sabido defender la salud del pueblo de Puerto Rico, ha velado por la pureza del arte y ciencia de practicar la medicina, y se ha enfrentado en forma vertical a los embates contra nuestra profesión, y por ende de nuestros médicos, sean asociados o no.

Esbozar en el día de hoy un mensaje programático de todas las actividades que se esperan llevar a cabo a lo largo de nuestro año de incumbencia, resulta arduo y un tanto académico, dado que mi gestión se encuentra enmarcada por las decisiones de todos ustedes, y está determinada por nuestra Junta de Directores y nuestra Cámara de Delegados, quienes marcan la pauta de la política pública de nuestra Asociación, que marcha paralela a la problemática del país en relación con los males sociales, la salud, práctica de la medicina y legislación.

Elaboraré algunos temas de importancia, para la consideración de todos ustedes.

A lo largo de toda la historia de nuestra Asociación, los intentos por parte del Estado de apoderarse de una forma u otra, de nuestras prerrogativas de médico, han sido claras y patentes, pero en esta década han sido más evidentes, sistemáticas y frecuentes las piezas legislativas que tratan de imponer medidas un tanto arbitrarias al libre ejercicio de nuestra práctica médica.

Después de un intento, a todas luces

descabellado de controlar y socializar en forma casi global la práctica de la medicina, finalmente el 23 de junio de 1976 fue aprobada la Ley 11, mediocre a todas luces, hoy, la base que regula en parte la práctica de la medicina en Puerto Rico, modificada en aquel entonces por la gestión que llevó a cabo nuestra Asociación, y no implementada en algunas de sus partes por lo inoperante de muchos de sus incisos y artículos.

Sin lugar a dudas, ha habido profusión de proyectos de ley sobre salud y reconocemos como los más desequilibrados los dos que intentaban regular el Tribunal Examinador de Médicos, 920 y 1117, y el menos conocido por ustedes para regular la práctica de la psicología, el 551, que son otros intentos poco afortunados de absorber y limitar nuestras ejecutorias como servidores públicos y que han movido a la Asociación Médica de Puerto Rico a levantar su voz ante todos nuestros médicos, nuestro pueblo, la Honorable Legislatura y nuestro Primer Ejecutivo.

Y para que no existan malos entendidos, seguiré hablando pero siempre teniendo ustedes presente el siguiente marco de referencia: "El derecho a disentir de los individuos o instituciones, es parte esencial de la buena democracia y este hecho, en ninguna forma o momento es sinónimo, ni se puede o se debe interpretar como hostilidad ni mucho menos politización",

Repito: "El derecho a disentir de los individuos o instituciones es parte esencial de la buena democracia y este hecho, en ninguna forma o momento es sinónimo ni se puede o se debe interpretar como hostilidad ni mucho menos politización".

Veamos, la capacidad eufemística o bue-

nas palabras de todos, pero sobre todo del Estado, no tiene límite.

Hay que dejar muy claro la importancia que para un país tiene la correcta planificación, gestión y control de su salud. Sabemos dónde estamos ubicados al presente, al contemplar las diversas medidas legislativas, no necesariamente encaminadas a unas libertades inherentes a la buena práctica de la medicina y salud del pueblo, y se proyectan hacia el futuro con una espada de Damocles puesta en nuestras cabezas.

La irritación que los proyectos de ley sobre materia de salud han ido suscitando entre los médicos, y la perplejidad que producen algunas medidas por parte de varias agencias del Estado, tratando de resolver los problemas de salud de nuestro pueblo, está llegando a un punto crítico.

Quien ha venido siguiendo la trayectoria de la Asociación Médica puede certificar que en cada caso concreto hemos procurado dejar patente nuestro punto de vista, y que, de cualquier forma nos ha animado en todo instante un especial y firme propósito de brindar a nuestro pueblo una mejor medicina, con la base de un análisis crítico de nuestras actuaciones ante cualquier esfera del Estado, o en otras facetas en las cuales nos vimos envueltos. Si no lo hiciéramos así caeríamos en una crasa beligerancia y tal como hicieron mis antecesores, tengo el firme propósito de defender la buena salud de nuestro pueblo a lo largo de todo este año, tratando de mejorar el camino para la solución de los problemas de salud de hoy y del futuro.

Nadie como el médico está más capacitado para comprender esta problemática y sin lugar a dudas los médicos constituimos una profesión de la mayor importancia y fuerza. La tendencia del Estado a ampliar su órbita en la medicina privada, es una trayectoria creciente hacia un evidente control sistemático y estrecho.

En este aspecto vemos esa continua tarea de asimilar totalmente los servicios de salud. Ante esta forma de reacionalización por parte del Estado tendremos que agotar nuestras mayores energías de oposición antes de que pueda ser impuesta la extensión, ampliación y engorde de las facultades del Estado, sobre nuestras propias ideas y decisiones en relación con la salud.

De lo contrario vamos a encontrarnos que tras no resolver los problemas de salud, los veremos incrementarse como consecuencia de la acumulación de equivocaciones de fondo.

No se trata de discutir ésta o aquella medida concreta, o de debatir tal o cual aspecto de la ley. Se trata básicamente de ver si las administraciones gubernamentales enfocan la política de salud que todos conocemos, y que resultaría sumamente tedioso enumerar ahora.

En el fondo, y no solo por razones económicas, sino primordialmente ideológicas, el Estado, aquí y en otros países, trata y tiende a adquirir todo el poder y nosotros aceptamos que tenga poder, pero no que lo tenga todo. Eso de tomar decisiones sin consulta previa y sin ajustarse a los moldes practicables para todos, es algo que ningún médico u otros ciudadanos en Puerto Rico aceptan de buen grado. Las experiencias llevadas a cabo en todo el mundo, con el objeto de lograr una mejor medicina a base de un control absoluto o socialización de la misma, no ha hecho sino registrar fracaso tras fracaso, tal vez porque la naturaleza humana no tiene entre sus ingredientes el de la perfección, y en vista de que la solidaridad espontánea no se produce, se ha venido intentando implantar la solidaridad obligatoria con la cual, si bien se mira, ésta no solo irá desapareciendo, sino que será imposible que se produzca, y no quedará margen para la libre determinación de ejercer generosamente la medicina.

El problema pues es uno de balance y control de los resortes del poder, tanto más



absolutos cuanto más intervengan en las decisiones particulares de los individuos o instituciones, y en este caso concreto, sobre nuestra Asociación Médica, nuestros profesionales y el bienestar y salud de nuestros enfermos.

Y si se apura la observación del fenómeno, el problema central es el de la elección de la libertad a costa de la igualdad, o la elección de la igualdad sacrificando la libertad. Este es un dilema que nunca tendría una respuesta del todo satisfactoria. Creo que sería un error el pensar que los proyectos del Estado constituyen o constituirán un cántico melodioso a las libertades del ejercicio de la medicina. Lejos de esto, los proyectos se dibujan siempre como el gran órgano burocrático que centraliza, coordina y aspira a gobernar la medicina en Puerto Rico, al extremo de intentar apoderarse de la autonomía de nuestro Tribunal Examinador de Médicos.

Si seguimos profundizando nos percatamos que todo se trata de no perder poder y las diferencias consisten en la intensidad de la dominación del aparato y en los distintos métodos empleados para ejercer ese control.

No estoy haciendo juicios de valor, sino limitándome a describir la realidad de la naturaleza humana, es un axioma que nadie abandona el poder político por propia iniciativa, ni lo abandona de buen grado. Siempre es precisa una especie de compulsión que obligue a quien tiene el poder a desprenderse de él. Por consiguiente, aceptado esto, nada tiene de extraño que todo gobernante tienda a mantener y a acrecentar su poder, y que la oposición intente despojarlo de él, pero sin lesionar los mecanismos que aspira a controlar algún día, y lamentablemente en medio de todas estas circunstancias políticas se encuentra la práctica de la medicina y la salud de nuestro pueblo.

Si analizan ustedes el cuadro resulta que ya no se ven con un poco de reflexión las co-

sas blancas o negras, sino que los grises en sus diversas tonalidades han hecho aparición.

Nosotros los médicos, los entendidos en la materia podemos decir categóricamente que con estas leyes concretas se está desperdiciando una gran oportunidad de hacer una ley razonable.

Como sabemos, la Asociación Médica de Puerto Rico tiene una gran capacidad de análisis en asuntos de salud y siempre tratamos de enfrentarnos táctica y técnicamente en las situaciones tendentes a contra-pesar como se pueda la posición del Estado, de la que se presume un alto grado de imperfección por principio, abalado además por la sólida experiencia que tenemos de las arbitrariedades y los errores de los gobiernos en general en materia de salud.

Si los gobiernos y el Departamento de Salud fuesen receptivos, acabarían aceptando algo de sus contradictores, aunque no sea todo, y el resultado de este pulso sería algo que no satisfaga a nadie pero tampoco sería para nadie totalmente rechazable. Recordemos en este momento la Ley 11 del 23 de junio de 1976.

Las manifestaciones en materia de salud de nuestra Honorable Legislatura han comenzado a producir el correspondiente alud de tinta de imprimir y hoy mismo es posible ya recopilar un dossier o album bastante voluminoso del tema que incluye todas las consideraciones expuestas por nosotros, otras entidades médicas y podemos determinar las diferencias que hay entre promesas y realidades. En buena lógica, no habría porque andar por la vida con suspicacias. Habría que confiar en la palabra, aunque sea una palabra política, que es como todos sabemos un poco menos palabra que las demás. Sin embargo, y como la benevolencia no significa estolidez (o fuera de razón) uno no puede remediar la duda razonable, aunque es bien cierto que nada desearíamos tanto como equivocarnos.

Todos entendemos la oposición de la

Asociación Médica de Puerto Rico ante las piezas legislativas 11, 920, 551 y otras más. Fue una oposición correcta, con una aceptación a medias por parte de la Honorable Legislatura en la Ley 11 y con un muy agradable éxito en los proyectos 920 y 551, cuando nuestro Primer Ejecutivo, con elementos de juicio finales fehacientes, aquilató con justicia y prudencia los pros y contras de estos proyectos y supo imprimir un veto a los mismos haciéndose evidente que nuestra disidencia a los proyectos era válida y lógica.

Pero además de la memoria, el entendimiento y los hechos nos permiten valorar una serie de datos que aumentan y confirman nuestro escepticismo a pesar de los vetos impartidos por nuestro Honorable Gobernador. Hace dos semanas llegó a la Asociación Médica de Puerto Rico el proyecto de Ley 1114 para reglamentar la práctica de la psicología y el mismo adolece de defectos similares al anterior 551.

¿Qué pasará ahora? ¿Qué ocurrirá en un futuro cercano? Levantemos un interrogante, pero muy a la expectativa de los acontecimientos por devenir.

Hay cosas en esta vida que para cambiarlas ameritan tiempo y lógica y los programas y soluciones de la medicina es uno de ellos, sobre todo cuando estos cambios los tratan de producir diferentes conductores o protagonistas, pero sin apearse del mismo automóvil oficial.

¿Qué harían ustedes si llegaran a ocupar puestos en la Legislatura o en la Secretaría de Salud? Parece la pregunta más lógica, pero en realidad es una de las preguntas más inútiles. Parece un sarcasmo más que una pregunta razonable. Ustedes estiman que la respuesta sería tan dulce y tan benévola como ustedes piensan ahora, ustedes serían absorbidos por el sistema o maquinaria política por dos razones fundamentales: primero, la motivación que los llevó a la política y, segundo, por postulados ideológicos partidistas. Esto no lo dice la Asociación Médica de Puerto Rico, lo dice la historia,

los hechos y las ejecutorias de quienes han ocupado estos cargos de las cuales tenemos conocimiento. Si analizamos al Estado a través de todos los partidos, vemos cuál es la clara tendencia en cuanto a materia de salud se refiere.

La contestación a la pregunta es sencilla, una cosa es lo que les gustaría y se confiesan capaces de hacer y otra es lo que pueden y tienen que hacer en medio de perspectivas políticas.

Por eso no es difícil adivinar qué medidas nos traerán nuevamente y por este motivo tenemos la obligación de estar en guardia, en pie firme y dispuesto a disentir de nuevo siempre y cuando nos respalde la verdad y la justicia.

Por todo lo expuesto es que nos anima el deseo de intentar cambiar en la Ley 11 todos aquellos aspectos que no son aceptables o adecuados a la salud de nuestro pueblo y a la práctica de nuestra profesión y espero la colaboración de todos sin distinciones ni divisionismos.

A base de los argumentos anteriores, es también nuestra opinión que ha llegado de nuevo a la mente de muchos de ustedes la idea de colegiación y algunos incluso hablan de sindicalización.

Los intentos de llevar a unos niveles de burocratización el ejercicio de la medicina gubernamental han llegado a unos límites muy difícilmente soportables por los propios médicos en muchos casos, obligados a convertirse en poco más que dispensadores de receta tras un triste simulacro de consulta supersónica, en pobres condiciones de trabajo, deficiencias, medios auxiliares y escasa remuneración y esto lo hemos podido comprobar durante el presente año en visitas por los distintos pueblos de la Isla. Hay que oír situaciones individuales y colectivas de muchos de nuestros médicos, situaciones increíbles y difíciles de comprender.

Sabemos que a lo largo de muchos años se ha oído el clamor de nuestros médicos gu-

bernamentales y muchas veces la Asociación Médica de Puerto Rico no ha podido envolverse en sus asuntos, pero en la actualidad con la aprobación por la Cámara de Delegados de la Asociación Médica de Puerto Rico se ha creado un consejo de médicos gubernamentales a nivel de nuestra Directiva Central, que estudiará, canalizará y elevará su voz a través de la Asociación Médica en todos los aspectos pertinentes que sean de nuestra incumbencia.

En estos días ha circulado en la prensa de Puerto Rico un aviso a las organizaciones de profesionales de la salud y cito: "A tenor con el Artículo 11 de la Ley 11 del 23 de junio de 1976, según enmendada, corresponde al Secretario de Salud designar por cada profesión de salud una Organización de Reglamentación y Evaluación Profesional. Delegará en cada una de ellas la facultad de preparar toda la reglamentación aplicable a sus respectivas profesiones en cuanto a la calidad de la prestación de servicios de los profesionales de salud incluyendo las estructuras que deban crearse para la evaluación de la práctica profesional".

En nuestras mentes no hay duda de que la Asociación Médica de Puerto Rico será elegida para esta labor, dado que reunimos los requisitos exigidos y contamos con la mayor matrícula dentro de la medicina organizada.

Analizaremos este aspecto de la ley y comenzaremos a laborar para emitir nuestra opinión y cumplir con nuestra tarea como asociación profesional.

Hoy día, nuestra Asociación reúne el 60 por ciento de los médicos del país, si lo comparamos con asociaciones de otras naciones nuestra cifra es adecuada y a la cima de la mayoría. En los Estados Unidos de Norteamérica la Asociación Médica Americana cuenta con un 49 por ciento de asociados del total de médicos de la nación y las cifras de asociados en otros países fluctúan dentro de este promedio.

Nosotros los puertorriqueños somos más ambiciosos y orgullosos dentro del campo de la medicina y de hecho tenemos uno de los mejores índices de salubridad en el mundo y estamos a la cabeza en las expectativas de vida.

¿Por qué nuestra Asociación no va a estar en la cúspide con el número de sus asociados? La gestión de atraer nuevos socios definitivamente es y tiene que ser a nivel personal, y así se ha demostrado en estos dos últimos años, con el ejemplo de algunas de nuestras sociedades de distrito.

La labor de cada uno de los miembros de nuestra Asociación es de suma importancia en este asunto, esta Asociación Médica de Puerto Rico a través de su Presidente les hace una petición formal, un compromiso que se puede llevar a cabo a lo largo de todo este año, cada uno de ustedes atraerá al seno de nuestra Asociación un médico idóneo. Es un reto que íntimamente debemos de aceptar y realizar.

### *Responsabilidad Social*

La Medicina es y debe ser una ciencia social. La relación que tiene y debe de tener la actividad propia del médico con la vida social es diáfana y precisa.

La actividad del médico debe de ser entendida desde la sociedad, en cuanto que ésta es la casa común del médico, del enfermo y de la relación entre ellos.

Les puedo indicar que todos los momentos integrantes del saber y del quehacer se hayan siempre condicionados por la sociedad que nos rodea, por la forma de vida y muy especialmente por el modo de hallarse envueltos el enfermo, el médico y la relación técnica entre ellos dentro de la sociedad de que somos parte.

La medicina, ciencia de la protección y de la conquista de la salud es en su esencia y en su más íntimo núcleo, una ciencia social, por lo tanto la vida social debe de ser entendida y en consecuencia tratada por el médico, así en su actividad normal como en sus anomalías,



puesto que sólo conociendo suficientemente lo normal de una vida puede ser conocido lo que de ella es patológico.

Aquí cabe recordar un párrafo del libro de "Mis Memorias" de Don Alejandro Tapia y Rivera, cito: "Mis compatriotas están enfermos, la inercia moral, la indiferencia, el egoísmo se los come, todo esto lo maldicen unos pocos sin poderlo remediar, muchos lo conocen, pero se contentan con maldecir", cierro la cita.

Lo que vio Don Alejandro a su regreso de España, ha ido en aumento, y ustedes saben que hoy, más que en el pasado, los problemas sociales en Puerto Rico son graves y serios y por este motivo, la Asociación Médica siempre consciente de su responsabilidad social con nuestros conciudadanos (pueblo) se ha proyectado en este sentido a lo largo de muchos años, pero ha sabido involucrarse en forma más abarcadora y sistemática a través de los esfuerzos llevados a cabo por el Comité de Calidad de la Vida, hoy comité permanente de la Junta de Directores. Siguiendo nuestra conocida trayectoria histórica como asociación, nos proponemos que nuestro Comité de Calidad de la Vida intensifique sus actividades al máximo, y al mismo se le adosarán nuevos horizontes, uno de ellos Problemas de los Envejecientes.

Este esfuerzo va encaminado a desarrollar destrezas en la representación de los envejecientes frente a organismos administrativos, mediante la implantación de estrategias de servicio a nivel nacional. Una parte importante de la labor a desarrollarse es la orientación y educación de la población en general, en áreas sustantivas del derecho del envejeciente.

Sus metas son: uno, mejorar las condiciones de vida del sector envejeciente indigente en Puerto Rico en los aspectos de ingresos, salud, vivienda, transportación y derechos civiles mediante el uso del instrumento legal; dos, tratar de eliminar los preconceptos y

el discrimen contra los envejecientes y estimular aquellos procesos comunitarios que propicien la integración del envejeciente a su comunidad; tres, facilitar la organización de la comunidad envejeciente con el fin de que pueda reclamar sus derechos.

El comité también se involucrará en el área de los impedidos, específicamente con los niños, la gama es grande, deficientes mentales, mudos, sordomudos, ciegos, etc.

Entendemos que no hay programas adecuados para ellos, y este aspecto sensitivo y álgido ha salido a la luz pública en estos días. Los derechos de estos niños están siendo violados, los sufrimientos de sus padres impotentes ante la situación, no tienen límite.

Apoyaremos y cooperaremos en la medida posible con los programas y entidades que tengan que ver con este asunto.

Estrecharemos fila luchando hombro con hombro con nuestro pueblo en contra de la violación, delincuencia, adicción a drogas, disolución de vínculos matrimoniales, que tan adversamente afectan nuestra sociedad.

Diremos presente en todo momento en lo que se refiere a calidad ambiental, ecología, cultura, historia, etc. Seguimos nuestras claras directrices, con otros proyectos y programas, siendo fieles a nuestros postulados como Asociación Médica, a saber, responsabilidad profesional, servicios de salud a los confinados, seguiremos cooperando con nuestro gobierno y con todas las agencias e instituciones que tengan en sus programas la discusión y prevención de los males sociales que afectan a Puerto Rico.

Tengan la seguridad y certeza que seremos fieles guardianes de la salud de nuestro pueblo, alzaremos la voz ante cualquier intento de coactar los buenos servicios médicos, velaremos porque se lleve a cabo una buena práctica médica y nuestro pueblo se sienta satisfecho con la misma.

Debemos mantener los costos por servicios médicos tratando de no elevarlos en la medida

posible.

No toleraremos ingerencia de ninguna índole cuando se trate de lesionar la relación médico-paciente.

Recabamos continuar siendo moderados y cautos, ajustándonos a nuestros cánones de ética en la forma de anunciarnos.

Mantendremos nuestro liderato en Educación Médica Continuada.

A lo largo de nuestra comunicación hemos tratado con bastante extensión el tema del Estado y su razón para legislar, cuál ha sido y debe de ser nuestra posición ante la legislación no acertada y frívola.

El por qué de intentar presentar modificaciones y legislación a la Ley 11 del 23 de junio de 1970.

El campo está abierto, el horizonte sin límites, el pueblo ávido y receptivo y nosotros, los profesionales médicos, tenemos la obligación individual y colectiva de ir cada día más lejos y ahondar en todos estos aspectos, proyectando, planificando, orientando, transmitiendo y tratando de canalizar a nuestro pueblo hacia un mejor estilo de vida.

Para finalizar, no quiero dejar a un lado el tema de nuestras escuelas de medicina.

De todos es conocido la gran cantidad de estudiantes puertorriqueños que salen al extranjero a estudiar nuestra profesión. Al presente en Puerto Rico tenemos la Escuela de Medicina de la Universidad de Puerto Rico, la Escuela de Medicina de la Universidad del Caribe en Cayey y la Escuela de Medicina de la Universidad Católica de Ponce. En el pasado respaldamos al igual que al presente su estable-

cimiento.

Es nuestra opinión que bien merece la pena involucrarse por parte de la Asociación Médica, en apoyar y afianzar en lo que sea posible a todas aquellas escuelas de medicina que reúna los requisitos adecuados y guarden los parametros de calidad exigidos y reconocidos por los organismos oficiales acreditadores de los Estados Unidos de Norteamérica y de nuestra Isla.

De todos es conocida la situación de la Escuela de Medicina de la Universidad Católica de Ponce. Resulta altamente contradictorio y paradójico que pueda perderse una entidad como ésta, que tanta falta nos hace y que fue creada con tanto sacrificio reconocida y acreditada desde sus comienzos.

Compañeros: Nuestro campo de acción Universal, nuestras proyecciones y ejecutorias deben de ser cada día más verticales, positivas y ambiciosas.

El esfuerzo a través de nuestros distritos, coordinados y al unísono.

Nuestras secciones de especialidades más activas.

Entiendo que cada uno de ustedes debe y tiene que mantener su individualidad, pero todos unidos en una sola meta, la salud de nuestros enfermos, a través de una práctica médica de excelencia.

Y todo esto por nuestro pueblo, por la salud de su gente, por nuestra profesión, por tí médico, por tu Asociación, por mi Asociación, por nuestra Asociación, inmensa y libre.

Muchas gracias.

## NOTA BIOGRAFICA



**GERARDO SANZ ORTEGA, MD**

*Presidente, Asociación Médica de Puerto Rico*

*1 9 7 9*

*Nació el doctor Sanz Ortega en Madrid, España, el 5 de noviembre de 1930. Sus estudios de medicina los realizó en la Escuela de Medicina de la Universidad de Salamanca, España, en donde obtuvo su Doctorado en Medicina y Cirugía en el año 1957.*

*Realizó su Internado en el Hospital de Distrito de Fajardo, Puerto Rico.*

*Se especializó en Siquiatría en el Centro Psiquiátrico para Investigación y Entrenamiento de la Escuela de Medicina de la U. P. R. durante los años 1959-1962.*

*Es miembro de la Asociación Médica Americana, de la Asociación Psiquiátrica Americana, de la Asociación Psiquiátrica del Caribe, de la Asociación Puertorriqueña de Graduados de Universidades Españolas y de la Asociación Americana de Práctica Profesional. Fue Presidente de la Sección de Siquiatría, Neurología y Neurocirugía de la AMPR, Vice-Presidente de la AMPR y Presidente de la Cámara de Delegados durante varios años.*



## PENSAMIENTO EN LA EPOCA NAVIDEÑA:

### RETABLO DEL SOLAR — ABELARDO DIAZ ALFARO SENTIDO CRISTIANO DE LA MEDICINA

Un hombre no es solo una entidad corporal. Es mente, corazón, espíritu, alma inmortal. Los males del hombre son de la mente, de la conciencia que le infectan la sangre, se la envenenan.. Es la sangre de Caín que llevamos en las venas....“Mens sana in corpore sano”, rezaba el adagio latino. Pero el cristianismo va más lejos. Conserva el cuerpo humano, que es la más maravillosa creación arquitectónica, como templo del espíritu. Más, si la escultura es la mujer hermosa y divina como mi tierra.

Un médico, en el sentido hipocrático o cristiano de la palabra, no brega solo con órganos, con fibras, huesos. Es una madeja de sueños, ilusiones, esperanzas. Recuerdo lo que me dijo el viejo maestro don Marce Román, cuando inconscientemente, amparándome en un frío objetivismo, mutilé la esperanza de Juana, que tenía el Peyo “descuidado, yendo y viniendo.”

—“Nunca mates la flor de una esperanza, cuando de la vida solo quedan ruinas.”—

Un médico debe serlo no solo de lo físico, de lo corporal. Físico como se le denominaba en castellano. Es médico y cirujano de la mente, que rige el cuerpo que lo gobierna, desde su alto tribunal. Debe ser médico de corazón. El corazón que para mí es el órgano más noble, más vital. Gautier Benítez, el bardo doliente, héctico de mi pueblo de Caguas, decía: “Allí vive la cabeza, aquí vive el corazón.” El más grande de todos los médicos, el Rabí de Galilea, afirmó categóricamente: “Allí donde estuviera vuestro tesoro estará vuestro corazón.” Lo primero que demandaba en los enfermos era que tuvieran confianza en El. En su poder sanador. Que tuvieran Fe, como un grano

de mostaza, y movería las montañas. Médicos hay que con su sola presencia consuelan, mejoran al paciente.. Que suelen ser impacientes. Había paralíticos, que de solo tocar la túnica del Maestro se sanaban. El médico es más que un mero profesional.

Para el Rabí de Galilea todos somos “obremos”. Clamó una vez: “Yo vine a servir y dar mi vida en rescate por muchos.”

Hipócrates establece un código de honor que no hay quien lo supere. Más que una profesión, la labor de médico es misión. En sus manos está la salud, la felicidad de una familia, de un pueblo. Tiene que hacer cuanto está a su alcance para curar el lacerado. Caminar las dos millas. Agotar todos los recursos disponibles humanos. ¡Nadie puede demandar, exigir que todos los enfermos, sanen!

El mismo Señor, no sanó o salvó a todos. Mas, si el paciente lo impide, no tiene fe, esperanza. Nadie se cura, si no tiene deseos, anhelos de vivir. Por eso un insigne patricio clamó: “Los pueblos como los individuos, cuando pierden el último rayo de luz de la esperanza o se degradan o se suicidan.”

El mismo Pedro, fue duramente reprimado por Cristo en la barca, cuando trató infructuosamente de caminar sobre la onda encrespada. —Hombre de poca Fe, ¿por qué dudaste?—

Recuerdo médicos del pasado, cuya memoria se perfuma con el incienso de nuestra gratitud. Médicos que formaban parte de nuestro hogar del íntimo y cordial sagrario de la familia. Médicos que sufren en carne propia nuestros dolores, enfermedades. Porque el médico trabaja con el dolor. Con la

carne dolorida y precaria. Con la mente conturbada. Es como una luz, como una esperanza que llega, que se prende junto al lecho de muerte. En el hogar, en los hospitales, en campo abierto, en el fragor cruento de la guerra, en las catástrofes y cataclismos. Es entonces el Buen Pastor "que su vida da por las ovejas". ¡Porque es ministro de Dios, instrumento eficaz, para la sanidad del cuerpo y la mente! Tienen ustedes un cuerpo honroso y de un preclaro abolengo. Deben sentirse orgullosos de tan esclarecido blasón y escudo de armas. Su aporte a la cultura, queda consignada a la maravillosa obra del Dr. Salvador Arana Soto. La lista, la nómina, el catálogo de nombres es insuperable, cimero.. Entre otros.... Zeno Gandía, Dr. José Antonio Dávila, Dr. José Gualberto Padilla, Dr. Tomás Blanco, Dr. Agustín Stahl, etc. Y un patriota que tiene un altar, un monumento en las conciencias de todos los hombres libres del mundo. Dr. Emeterio Betances, que combatió la esclavitud del hombre, de los pueblos, que es enfermedad letal, fatal, que mina las fuerzas anímicas y espirituales de los seres.

El médico cumple una misión trascendente. Una función sagrada.. Trabaja con carne torturada, mutilada, triste. El insigne novelista, Eduardo Mallea, que veneraba su padre médico de provincia rural, decía: "Mi padre trabaja con la carne triste."

El médico encierra ese espíritu cordial, de abnegación y sacrificio, ese sentido místico, humanizado, cristiano de la medicina. Y pido a Dios, que se perfeccionen los instrumentos para facilitar la cura de los seres. Que no se escatime, que no se tacañee, que no se juegue con la salud, de los de la carne triste.. Especialmente la de los niños enfermos. Que miran la vida desde las últimas claraboyas. Que no cantan, que no juegan, que no ríen. Como los pájaros enjaulados o heridos.

Nadie enfermo puede gozar a plenitud la vida.

Confío en ustedes. Se que es una clase preocupada, por el destino de su pueblo. Su deferencia y reconocimiento hacia mí es notoria. Y agradecimiento es virtud jíbara.

Lo normal en el hombre no es la salud. Nacimos enfermos. Y saludamos la vida, no con risa, sino con llanto. El dolor está constante en el hombre. ¡Hay que vencer el dolor, y triunfar sobre la muerte! Recuerdo lo que dijo don Marce Román: "Nunca mates la flor de una esperanza, cuando de la vida solo quedan ruinas..." y el médico es la Fe y la Esperanza.

Narró: Rey Francisco Quiñones  
Octubre de 1979

## ABSTRACTOS DE LITERATURAMEDICA

### THE AGING INTERVERTEBRAL DISK:

*Sandy L. Burkart, PhD - Physical Therapy, August, 1979.*

El disco intervertebral envejeciente. El tejido de las articulaciones tiende a absorber y redirigir fuerzas potentes que son generadas en el esqueleto por los músculos y la gravedad.

Los tejidos resisten fuertes cargas debido a la matriz extracelular que contienen.. Cada matriz de tejido conectivo está formado por una mezcla típica de los cuatro componentes que la forma: Agua, células, productos celulares como elastina y colagen y además proteoglycanos. La matriz adquiere fuerza de la fibra colagen, elasticidad de la elastina y resistencia a la presión del agua que se encuentra químicamente unida a los proteoglycanos y que no puede difundir.

El disco intervertebral joven está formado por una capa laminada exterior llamada anillo fibroso. Cada lámina se forma de fibras colágenas que se unen firmemente a las vértebras adyacentes. El anillo se continúa con una sustancia gelatinosa llamada núcleo pulposo. Este consiste de algunas células, fibras colágenas pero principalmente proteoglycanos unidos al agua. El disco no tiene inervación y solamente la región anular tiene vasos sanguíneos. A medida que el disco envejece la distinción entre el anillo fibroso y el núcleo pulposo se pierde debido a la pérdida de agua de su contenido. En cualquier momento mientras el disco está viscoso puede fluir el núcleo a través del anillo y herniarse comprometiendo las estructuras a su alrededor.

El disco deshidratado y prolapsado nunca asumirá su forma y posición original. Constituye una de las estructuras del aparato músculo esquelético espinal de degenera con el envejecimiento. Se han hecho estudios para poder detectar la patología tanto a nivel microscópico como molecular. Se cree que la célula no puede sintetizar los materiales que forman la ma-

triz en suficiente cantidad y calidad, ya que dependen de la difusión a través de la matriz densa para su nutrición. Esta matriz está deshidratada y en degeneración por lo que no constituye un medio adecuado para la difusión. A pesar de estas dificultades de la célula aun no se ha encontrado que existan defectos celulares que lleven a la degeneración.

La investigación en este campo está impedida por muchos variantes de los cuales se encuentran la falta de obtención de material humano.

(Sometido por Tomás Poventud, MD)

### EPIDEMIOLOGY OF HIP FRACTURE

*Hielema, F.. J. Physical Therapy, 59: 1221-1225, 1959 .*

Las fracturas de cadera hacen el número 55 en frecuencia diagnóstica pero son el número 10 en utilización de dias-hospital. En revisión de la literatura se encuentra relación íntima de este diagnóstico con la edad avanzada. Aunque la mujer es afectada en mayor número que el hombre, a éste le ocurre a menor edad. Se implican muchas condiciones y usos de medicamentos como asociadas a las fracturas de caderas pero ninguna en prominencia marcada.. Algunos factores tales como ingestión de fluoruro, actividad física vigorosa, vitamina D y calcio apropiadas en la dieta y exposición a luz solar, se implican como retardadores de osteoporosis y por ende reductores del riesgo de fracturas.

Se desprende de esta revisión que la gran mayoría de las fracturas de cadera están resueltas a un año plazo regularmente. Sin embargo, se encuentra que factores tales como la falta de cónyuge, vida muy se-



dentaria anterior a la fractura, syndrome orgánico, edad sobre 75 años retardan o impiden la recuperación del paciente. Hay varias fórmulas, tablas, etc. desarrolladas para ayudar en predecir las posibilidades de éxito en la rehabilitación de los afectados, ninguna con mayor prominencia que otras en su uso.

El conocimiento de los factores que rodean el paciente antes y después de la fractura son importantes para todos los profesionales que se envuelven en el tratamiento a corto o largo plazo para determinar el curso de acción más conveniente.

(Sometido por Frank W. López, MD)

## CHARACTERIZATION OF ATRIAL FLUTTER

27 patients who developed atrial flutter in the immediate period after open heart surgery were studied, using the epicardial surface or the superior portion of the right atrium where bipolar atrial wire electrodes were placed. Two types of atrial flutter were identified: type I or classic A.F. (rates 240 to 338 beats/min.) and type II A. F. (rates 340 to 433 beats/min.). In the first group the atrial rhythm could be interrupted by rapid atrial pacing in the right atrium, in the second group could not. As with Type I atrial flutter, type II A. F. was characterized by a constant beat-to-beat cycle length, morphology, polarity and amplitude of the recorded atrial electrogram. Beat-to-beat electrical alternans sometimes associated to alternans in beat-to-beat cycle length was found in both groups. Two patients with type II A. F. changed to type I A. F. in a stepwise fashion which does suggest that they are not really the same.. Four cases showed type II A.F. upon cessation of rapid atrial pacing initiated to treat type I A. F. Perhaps type II A. F. represents an intermediate rhythm between atrial fibrillation and type I A. F.

In summary the mechanism of either type I or type II atrial flutter is incompletely understood whether be it re-entry, automatic focus, triggered activity or

something else. It is possible that a focus generating a rapid regular rhythm may be responsible for atrial flutter (type I or II) or to atrial fibrillation when it is so fast that the entire atria cannot respond in a 1:1 fashion.

(Sometido por Dr. Couto)

## REACTIVACION DE TUBERCULOSIS DESPUES DEL REEMPLAZO TOTAL DE LA CADERA

*J. of Bone and Joint Surgery 61-B 148 (5, 1979)*

El reemplazo total de la cadera puede conducir a la reactivación de la tuberculosis. El autor describe dos historias clínicas de dos pacientes que desarrollaron tuberculosis de la cadera durante la niñez. Ambos pacientes fueron tratados con inmovilización sin tratamiento antituberculoso alguno. Después de 35 y 41 años estos pacientes fueron sometidos a cirugía de reemplazo en una o dos caderas a causa del arca interior en las articulaciones.

Doce meses después de la cirugía en un paciente se desarrolló una masa en el muslo izquierdo que se extendió a la cápsula de la cadera. Se cultivó M. Tuberculosis de la herida. Al desarrollar alergia a las drogas antituberculosas la prótesis fue removida. El otro paciente desarrolló una fístula de la cadera derecha de la cual se cultivó M. tuberculosis. Con tratamiento específico (INH, RMP, EMB) el paciente está mejorando.

Los autores recomiendan que en pacientes con historial previo de tuberculosis se inicie terapia antituberculosa inmediatamente antes de la cirugía de artroplastia y se continúe por lo menos por doce a dieciocho meses después.

(Sometido por Ramón E. Figueroa Lebrón, MD)

**FIEBRE INDUCIDA POR IZONIAZIDA***Chest 75: 2*

Las reacciones febriles asociadas al uso de izoniazida pueden ser una complicación de esta terapia. El comienzo de la fiebre usualmente se presenta luego de varios días de comenzado el tratamiento y lleva asociadas evidencias de hipersensibilidad tales como erupciones cutáneas, eosinofilia, elevación de inmunoglobulina E y a veces elevación de las enzimas hepáticas. En este artículo se presenta un paciente que se le comenzó la administración de izoniazida luego de convertir la prueba de tuberculina cutánea y antes de comenzarse la quimioterapia para carcinoma. Desde la primera dosis de la droga el paciente exhibió náuseas, vómitos, escalofríos y una temperatura que varió entre 38 y 40° grados.

Cada vez que se trataba de comenzar la droga el paciente exhibía el mismo cuadro febril con los otros síntomas arriba indicados.

La fiebre y los demás síntomas desaparecían una vez era suspendida la administración de izoniazida. En ninguna de las ocasiones hubo evidencia sistémica de hipersensibilidad a la droga.

Este reporte es importante porque subraya la posibilidad de que izoniazida pueda ser la responsable de un cuadro febril en un paciente que la está recibiendo aún cuando solo haya sido una dosis única.

(Sometido por Ramón E. Figueroa Lebrón, MD)

**ACUTE HEMODYNAMIC EFFECTS OF CIGARETTE SMOKING IN MAN ASSESSED BY SYSTOLIC TIME INTERVALS AND ECHOCARDIOGRAPHY**

*Rabinowitz, BD, Thorp, K, Huber, GL, Abelmann, WH. Circulation 60: 752, 1979.*

El propósito de este estudio fue investigar los efectos del cigarrillo en la hemodinámica y función

del ventrículo izquierdo. Se estudiaron 16 pacientes de edades de 18 a 35 años antes y después de fumar cigarrillos de alto contenido de nicotina y de bajo contenido de nicotina. Los estudios hechos fueron mediante ecocardiografía e intervalos sistólicos. Ambos tipos de cigarrillos aumentaron el pulso, presión arterial y disminuyeron la razón de período pre ejetivo a período de eyección del ventrículo izquierdo. Ambos cigarrillos aumentaron la contractilidad del ventrículo izquierdo. Los cigarrillos altos en nicotina aumentaron el tamaño diastólico del ventrículo izquierdo mientras que los cigarrillos bajos en nicotina disminuyeron el volumen sistólico del ventrículo izquierdo. Concluyen los autores que el fumar un cigarrillo alto en nicotina aumenta todos los factores que determinan el consumo de oxígeno del miocardio y aumenta el retorno venoso al corazón. La data también sugiere que el humo del cigarrillo contiene sustancias no nicotínicas con efectos inotrópicos y cronotrópicos.

(Sometido por G. Cintrón, MD, VAH)

**EMG COMPARISON OF QUADRICEPS FEMORIS ACTIVITY DURING KNEE EXTENSION AND STRAIGHT LEG RAISES**

*Knight K., Martin J., Londeree, R., Vol. 58 No. 2: 57: 68 - Am. Jour. Phys. Med., April, 1979.*

Ambos ejercicios, extensión de rodilla y elevación de la pierna con la rodilla en extensión, han sido utilizados para rehabilitar la musculatura atrofiada del cuádriceps después de períodos de inmovilización de la rodilla. Utilizando EMG, para medir el desarrollo de tensión en segundos. Se hizo un estudio en ambos ejercicios para comparar las tensiones desarrolladas en el cuádriceps en 3 niveles diferentes de actividad (20 por ciento, 50 por ciento, 80 por ciento). La tensión desarrollada fue significativamente mayor durante extensión de la rodilla. Para ambos ejercicios y en los 3 niveles de actividad en el músculo más activo fue el vasto lateral y el menos activo el vasto medial. La diferencia de tensión entre ambos ejercicios

aumenta a medida que aumenta el nivel de actividad. Por tanto, a menos que esté contraindicado por la presencia de condromelacia, la extensión de la rodilla debe ser utilizada para la rehabilitación post-quirúrgica de la rodilla. A mayor desarrollo de tensión más rápidamente regresará la fuerza y por tanto más rápida la rehabilitación.

(Sometido por Jesús A. Maldonado, MD)

## MANAGEMENT OF RHEUMATOID ARTHRITIS WITH ORAL GOLD

*Weisman M., Hannifin, D., Arthritis and Rheumatism, Volume 22 No. 8 - 922-925, August, 1979.*

En los primeros meses del "trial" sin control, fuera de los Estados Unidos, en el manejo y tratamiento de pacientes con artritis reumatoidea utilizando el nuevo absorbible y administrado oralmente compuesto conteniendo oro, se ha demostrado que la droga Auranoquina es bien tolerada, segura y efectiva. Una preocupación potencial, sin embargo, fue la observación de que dosis administradas de 6 a 9 mg. por día, estaban asociadas con una alza progresiva de los niveles de oro en la sangre, sugestivo de un balance neto "positivo" y con una continua acumulación de oro dentro del cuerpo.

Según los autores Weisman y Hannifin, un estudio reciente realizado por ellos en los Estados Unidos por un año y con un mayor número de pacientes con el propósito de aumentar información sobre la eficacia y toxicidad de Auranoquina, demostró que, ésta, a dosis menores y de 4 mg/día, está asociada con regresión de la actividad de la enfermedad en 2/3 de los pacientes y de que no hay evidencia de toxicidad significativa o de acumulación progresiva de oro en el cuerpo.

Si la terapia de oro por vía oral trabaja terapéuticamente tan bien como la crisoterapia y sin sus frecuentes efectos marginales y molestias, representaría un avance mayor en el manejo de pacientes con artritis reumatoidea.

(Sometido por Rafael Alvarez, MD)

## CURRENT CONCEPTS IN MANAGING TIA'S AND STROKE

*Melvin, G., Geriatrics, 39: 9: 53-54, April 1979.*

Aunque no hay daño neurológico permanente luego de un ataque isquémico transitorio, pacientes con esta sintomatología están a riesgo de una apoplejía. Los ataques isquémicos transitorios se caracterizan por su desarrollo rápido, se maximiza a los 5 minutos de haber empezado y es de una duración variable entre 2-15 minutos usualmente, tan largos pero no mayor que 24 horas y tienen una disolución rápida. El artículo procede con el diagnóstico diferencial del AIT, versus el desarrollo de una apoplejía (área focal de isquemia.) El tratamiento exitoso de un AIT depende de identificar el factor que precipite este cuadro sea el corazón, la sangre, o la pared del vaso. Usualmente se emplean drogas como anticoagulantes y antiplaquetación en los casos de etiología sanguínea o de enfermedad arterioesclerótica del vaso. Estas drogas se dice, reducen la incidencia del AIT pero no de un ataque apopléjico. El ataque apopléjico en desarrollo se trata con heparina en las primeras 29-78 horas para minimizar los daños del infarto excepto en los casos en los cuales la etiología es hipertensión o policitemia.

(Sometido por José A. Arabia, MD)

## EARLY MOBILIZATION OF PATIENTS WITH UNSTABLE FRACTURE, OF THE THORACIC AND LUMBAR SPINE, A TWO YEAR FOLLOW-UP

*Hein Sorensen, O., Nachemson, A. - Scand. J. Rehab. Med. 11: 47-61, 1979.*

Durante el período de inmovilización aguda 18 pacientes con fracturas inestables de la columna vertebral acompañadas casi siempre de lesión al cordón espinal caudal a T<sub>2</sub> se movilizaron usando una mesa inclinable "tilt table". Doce de estos pacientes se empezaron a movilizar después de la segunda semana del accidente y se llegó a 30° de inclinación a los 15 días, 50° a los 37 y 90° a los 65 días post fractura. A todos



los pacientes se les dio seguimiento por 2 años. Una comparación entre pacientes con daño similar tratados conservadoramente y el grupo de pacientes de movilización temprana no demostró diferencias respecto a deformidades de la columna vertebral, daño al cordón espinal o a los síntomas subjetivos del paciente.

Se concluye que es beneficioso para el paciente con fractura vertebral caudal a T<sub>2</sub> tenga o no daño al cordón la movilización temprana a partir de la segunda semana, ya que nos evitaremos las complicaciones de la inmovilización prolongada.

(Sometido por José A. Arabia, MD)

#### ACTIVATION OF ABDOMINAL MUSCLES DURING SOME PHYSICAL THERAPEUTIC EXERCISE.

El propósito del estudio es evaluar la eficiencia de algunos ejercicios para desarrollar la fuerza de los músculos abdominales. Se encontró que el "sit-up" con la espalda arqueada estimula el rectus abdominis y el oblicuo abdominis a un 50 por ciento de su valor máximo medido electromiográficamente. Este ejercicio se comparó con otros dos ejercicios sugeridos para el desarrollo abdominal. Esos son, el "sit-up" con activación simultánea de los flexores plantares del tobillo y el "sit-up" con la espalda hyperextendida. Se encontró que ninguno es superior a los otros en cuanto a activación de los músculos abdominales. Se encontró que el "sit-up" con rotación lateral del tronco daba una alta activación a los oblicuos abdominales.

(Sometido por José A. Arabia, MD)

- Feb. 2-8: 18th Annual Seminar, "Imageology 1980", Fontainebleau Hilton, Miami Beach, FL. Sponsored by Dept. of Radiology, Mt. Sinai Medical Center. Program director, Dr. Manuel Viamonte, Jr. Inquiries: Miami Seminars, PO Box 343762, Coral Gables, FL 33134.
- Feb. 8-11: Decision-Tree Approach to Diagnostic Radiology. Dutch Inn, Lake Buena Vista, FL (Walt Disney World). Sponsored by Dept. Radiology, Mount Sinai Medical Center, Miami Beach, FL. Dr. Manuel Viamonte, Jr., program director. Inquiries: (See Feb 2-8).
- Feb. 12-15: AHA Council on Circulation Scientific Sessions. Keystone, CO. Robert Zellis, MD, course director. Inquiries: AHA, 7320 Greenville Ave., Dallas, TX 75231, tel. 214-750-5441.
- Feb. 18-22: Nuclear Cardiology In-Service Workshop. Univ. Miami (FL) School of Medicine, Aldo N. Serafini, MD, director. Inquiries: Dr. Serafini, PO Box 016960, Miami, FL 33101.
- Feb. 21-23: 5th Joint Meeting on Stroke and Cerebral Circulation. Buena Vista, FL (Walt Disney World). Sponsored by AHA Stroke Council, Cerebrovascular Surgery Section American Association of Neurological Surgeons, Canadian Stroke Society and Society for Vascular Surgery, Drs. Robert G. Siekert and J. Donald Easton co-directors. Inquiries: Postgraduate Programs, AHA Headquarters, Dallas, TX 75231.
- Feb. 24-29: Controversies and Advances in Radiology and Medicine. Jeffersonville, VT. Sponsored by Tufts University School of Medicine. Inquiries: Tufts, 136 Harrison Ave., Boston, MA 02111, Tel. 617-956-6578.
- Feb. 25-26: 11th Annual Nephrology Conference, San Antonio, TX. Sponsored by AHA. Drs. Jay H. Stein and H. John Reineck, course directors. Inquiries: AHA, 7320 Greenville Ave. Dallas, TX 75231, Tel. 214-750-5441.
- Feb. 27-29: Cardiology for Nurses. Georgia Baptist Medical Center, Atlanta, Drs. G. F. Fletcher, J. D. Cantwell, and Barbara Johnston, M. N. co-directors. Inquiries: Dr. Fletcher, Georgia Baptist Med. Cent., 300 Blvd. NE, Atlanta, GA 30312.
- Feb. 27-Mar. 1: Contemporary Management of Stroke and Coronary Disease. Taos, NM. Inquiries: W. J. Levy, MD, Symposia de Santa Fe, PO Box 5175, Santa Fe, NM 87502. Tel. 505-982-1911.
- Feb. 28-29: Northwest Stroke Symposium. Washington Plaza Hotel, Seattle, WA. Inquiries: Northwest Hospital, 1551 N. 120th St. Seattle, WA 98133. Tel. 206-364-0500 Ext. 686.
- Feb. 29-Mar. 2: 3rd Annual Intensive Clinical Neurology Course for Non-Neurologists. New York City. Inquiries: Dr. L. P. Levitt, course director, 1033 Hamilton St., Allentown, PA 18101. Tel. 215-433-6474.
- Mar. 3-5: 20th Annual Conference on CVD Epidemiology. Islandia Hyatt House, San Diego, CA. Sponsored by AHA Council on Epidemiology and NHLBI. Dr. L. Kuller, program chairman. Inquiries: Scientific Sessions, AHA National Center, 7320 Greenville Ave., Dallas, TX 75231.
- Mar. 9-12: 54th Congress, International Anesthesia Research Society. MGM Grand Hotel, Reno, NV. Inquiries IARS, 3645 Warrensville Center Road, Cleveland, OH 44122.
- Mar. 9-13: 29th Annual Scientific Sessions, American College of Cardiology. Houston, TX Civic Center. Inquiries: ACC, 9111 Old Georgetown Rd., Bethesda, MD 20014. Tel. 301-897-5400.
- Mar. 15-16: Relevance of HLA and Clinical Medicine. San Diego Hilton. Sponsored by UCSD. Inquiries: Off. Cont. Ed. M-017, UCSD School Medicine, La Jolla, CA 92093.
- Mar. 16-19: Basic Cardiology for Practicing Physician. Ahwahnee, Yosemite National Park. CA. Sponsored by Dept. Med. Div. Card. and Ext. Progr. in Med. Ed. UCSF School of Medicine. Inquiries: Room 569-U, UCSF, 3rd and Parnassus, San Francisco, CA 94143, Tel. 415-666-4251.
- Mar. 23-25: 6th National Conference on High Blood

Pressure Control. Shamrock Hilton, Houston, TX. Dr. Ray W. Gifford, Jr. chairman. Inquiries: NCHBPC, 1501 Wilson Blvd., Suite 600, Arlington, VA 22209, Tel. 703-527-4500.

Mar. 27-30: Workshop in Echocardiography. Don Cesar Beach Hotel, St. Petersburg Beach, Fl. Dr. L. E. Teichholz, director. Inquiries: B. N. Chiles, Tampa Tracings, PO Box 1245, Tarpon Springs, FL 33589.

Apr. 1-4: Critical Care Medicine. Medical College of Georgia, Augusta. Sponsored by Medical College of Georgia. Inquiries: Dr. Gerald T. Chambers. Div. Cong. Ed. Medical College of Georgia, Augusta, GA 30912. Tel. 404-828-3967.

Apr. 10-12: Clinical Approach to Exercise Testing. Sheraton-Sand Key Hotel, Clearwater Beach, Fl. Dr. S. P. Glasser and P. I. Clark, R. N. co-directors: Sponsored by Tampa Tracings and Univ. of South Flor. Dept. of Med. Inquiries: B. N. Chiles, Tampa Tracings, PO Box 1245, Tarpon Springs, Fl. 33589.

Apr. 13-17: Annual Meeting, Association for Advancement of Medical Instrumentation. Hyatt Embarcadero, San Francisco, Inquiries: AAMI, 1901 N. Ft. Myer Dr. Arlington, VA 22209. Tel. 703-525-4890.

Apr. 14-17: Federation of American Societies for Experimental Biology. Anaheim, CA. Inquiries: B. C. Nichols, 9650 Rockville Pike, Bethesda, MD 20014.

Apr. 17-19: National Conference on Cancer Prevention and Detection. Palmer House, Chicago. Sponsored by American Cancer Society, Inquiries: Dr. N. G. Bottiglieri, ACS, 777 Third Ave., New York, NY 10017, Tel. 212-371-2900.

Apr. 21-23: 17th Annual Rocky Mountain Bioengineering Symposium. U.S. Air Force Academy, Colorado Springs, CO. (Abstract by Dec. 15, 1979). Inquiries: David R. Carroll, MD, Dept. Elec Engineering. USAF Academy CO 80840, Tel 303-472-3190.

Apr. 23-29: Annual Meeting, North American Society for Cardiac Radiology. Mark Hopkins Hotel, San Francisco. Inquiries: Erik Carlsson, MD, UCSF School Med. Dept. Radiology, San Francisco, CA 94143.

Apr. 28-30: Annual Meeting, American Association

for Thoracic Surgery. San Francisco Hilton, Inquiries: AATS, 6 Beacon St., Boston, MA 02108.

Apr. 30: Hypertension: Evaluation and Treatment. Towsley Center, University of Michigan Medical School. Inquiries: Off. Cont. Med. Ed. Towsley Center, U. of Mich. Med. School, Ann Arbor, MI 48109.

May 6-8: 7th Annual Symposium for Coordinating Clinical Trials. Philadelphia. (Abstracts by Jan. 21, 1980) Sponsored by Society for Clinical Trials, Inquiries: Dr. C. R. Klimt, SCT, 600 Wyndhurst Ave., Baltimore, MD 21210.

May 7-10: AHA Great Teachers Conference-East Coast. Hot Springs, VA. Inquiries: AHA Postgraduate Course, National Headquarters, 7320 Greenville Ave., Dallas, TX 75231.

May 11-14: 7th Annual Scientific Meeting, International Society of Hypertension. New Orleans. Inquiries: Edward D. Frohlich, MD, Alton Ochsner Medical Foundation, 1516 Jefferson Highway, New Orleans, LA 70121. Tel. 504-831-2037.

May 15-18: 24th Annual Meeting American Society of Internal Medicine. Washington, DC. Inquiries: ASIM, 2550 M St. NW, Washington, DC 20037, Tel. 202-659-0330.

May 18-21: Joint Annual Meeting, American and Canadian Thoracic Societies. Washington, DC. Inquiries: Dr. W. W. Addington, ATS/CTS, 1740 Broadway, NY, NY 10019.

June 5-6: 10th Annual Postgraduate Course Neurosurgery, Hilton San Francisco. Sponsored by University of California San Francisco Neurosurgery Dept. Inquiries: S. G. Medaxian, Neurosurgery, UCSF, San Francisco, CA 94143.

June 11-13: 3rd Annual Meeting, Shock Society, Lake Ozark, MO. Inquiries: Dr. Lerner B. Hirshan, VA Hospital, Oklahoma City, OK 73104.

June 17: Subspecialty Exams for Nephrology, Pulmonary Disease, Hematology. Inquiries: American Board of Internal Medicine, University City Science Center, 3624 Market St., Philadelphia, PA 19104, Tel. 215-243-1500.

Oct. 6-10: 5th International Pediatric Nephrology Symposium. Philadelphia. Co-hosts: Children's Hospital Philadelphia and St. Christopher's Hospital for Children. Inquiries: Dr. Michael E. Norman, Room 6237, Children's Hospital Philadelphia,



- 34th & Civic Center Blvd. Philadelphia, PA 19104.
- Oct. 19-24: Clinical Congress American College of Surgeons. Atlanta. Inquiries: ACS, 55 E. Erie St., Chicago, IL. 60611.
- Oct. 25: 3rd Recertification Examination in Internal Medicine. Various test centers. Inquiries: American Board Internal Medicine, 3624 Market St., Philadelphia PA 19104.
- Nov. 17-20: 53rd Annual Scientific Sessions, American Heart Association, Miami Beach, FL. Inquiries: Scientific Sessions Section, AHA, 7320 Greenville Ave., Dallas TX 75231.

## ABROAD:

### 1980

- Mar. 23-27: Spring Meeting, American College of Surgeons, Toronto, Canada. Inquiries: ACS, 55 E. Erie St., Chicago, IL. 60611.
- Apr. 8-12: First World Biomaterials Congress. Baden near Vienna, Austria. Inquiries: E. Maurer, Medical Academy of Vienna, Alser Strasse 4, A-1090 Vienna, Austria. Cable: MEDACAD Wien.
- Apr. 9-11: 12th European Congress for Non-Invasive CV Dynamics. Athens, Greece (Abstracts by Jan. 1, 1980 in Athens) Inquiries: Hellenic Cardiological Society, 17 Sisini St., Athens, 612, Greece.
- Apr. 11-13: 46th Annual Scientific Meeting German Society for Circulation Research. Bad Nauheim, Germany. Inquiries: prof. Dr. W. Schapter, Deutsche Gesellschaft fur Herz-und Kreislaufforschung. Max-Planck-Institut fur physiologische und klinische Forschung, W. G. Kerckhoff-Institut. D-6350 Bad Nauheim 1, West Germany.
- Apr. 19-23: 2nd Pan American Congress on Diseases of the Chest. Hotel Nacional, Rio de Janeiro, Brazil. Inquiries: Jesse P. Teixeira, MD, CP 370, Rio de Janeiro, R. J. 20000, Brazil.
- June 2-6: World Congress of Paediatric Cardiology. London, England. Inquiries: Conference Secretariat, 4" L" Portman Mansions, Chiltern St., London, W1M 1LF, England.
- June 3-6: 2nd International Symposium on Computers in Critical Care and Pulmonary Medicine. Lund, Sweden. Inquiries: B. Richardson, Kliniskt Fysiologiska Avdelningen, Lasarettet, S-221 85

- Lund, Sweden.
- June 16-19: 1st Asian-Pacific Symposium on Cardiac Pacing. Jerusalem, Israel. Sponsored by the Asian-Pacific Society of Cardiology. Prof. Henry N. Neufeld, chairman, organizing committee. Inquiries: PO Box 16271, Tel. Aviv, Israel.
- June 22-26: 8th European Congress of Cardiology. Paris, France., Inquiries: Congress Cardiologie P.M.V. B P. 246, 92205, Neuilly-s-Seine, France.
- June 23-26: 71st Annual Conference, Canadian Public Health Association. Skyline Hotel, Ottawa, Ontario, Canada. (Abstracts by Dec. 31, 1979) Inquiries: CPHA, 1335 Carling Ave., Suite 210, Ottawa, Ont., Canada K1Z 8N8.
- July 8-11: The Cardiac Electric Field-Its Measurement and Modelling. Dresden, Germany. Associated with 28th International Congress of Physiology. Inquiries: Prof. E. Schubert, Humboldt-University, 3-4 Hessische Str., 104 Berlin, Germany.
- July 23-24: International Symposium, Prostaglandins and the Kidney. Stuttgart, West Germany. Associated with 28th International Congress of Physiology. Inquiries: Dr. J. C. Frolich, Fisher-Bosch-Institut of Clinical Pharmacology. Auerbachstr. 1113, D-7000, Stuttgart, West Germany.
- July 23-25: 2nd International Symposium on Mechanisms of Vasodilatation. Wilrijk, Belgium. Associated with the 28th International Congress of Physiological Scientists. Inquiries: Ms. L. Van den Eynde, Dept. Geneeskunde, Universitaire Instelling Antwerpen, Universiteitsplein 1, B-2610 Wilrijk, Belgium.
- Aug. 4-6: 12th Biennial Congress, Southern Africa Cardiac Society. Johannesburg, South Africa. Inquiries: Division of Cardio-thoracic Surgery Medical School, University of Witwatersrand, Hospital St. Johannesburg-2001, South Africa.
- Aug. 16-29: 13th International Teaching Seminar on Cardiovascular Epidemiology and Prevention. Kaunas, Lithuanian SSR. Application before March 15, 1980. Inquiries: Rose Stamler, Epidemiology Council, ISFC, 303 E. Chicago Ave., Room 1-615, Chicago, IL. 60611.
- Sept 7-13: Interamerican Congress of Cardiology. San Juan, Puerto Rico. Inquiries: GPO Box 3886, San Juan, PR. 00936. Tel. 809-764-4219, Cable PRINTERCAR.
- Sept. 14-17: 5th International Symposium on Micro-

surgical Anastomoses for Cerebral Ischemia. Vienna Hilton, Vienna, Austria. Inquiries: Prof. Dr. W. Th. Koos, Dept. Neurosurgery, University of Vienna, Alser Str. 4 A-1090 Vienna, Austria.

Sept. 22-26: 3rd Asean Federation of Cardiology Congress. Mandarin Hotel, Singapore, Rep. of Singapore. Sponsored by Sing. Ministry of Health, Academy of Medicine and National Heart Association. Inquiries: Dr. J. H. H. Sheares, Academy of Medicine, 4-A College Rd., Singapore, Rep. of Singapore.

Sept. 23-28: 10th Heart Congress of International Society for Heart Research. Moscow, Inquiries: Prof. V. N. Smirnov, National Cardiology Research Center, Academy of Medical Sciences, Petroverigsky Lane 10, Moscow 101882, USSR.

Sept. 29-Oct. 1: 6th Annual Meeting. European Society for Artificial Organs. UNI II, Geneva, Switzerland, Inquiries: Dr Jacques Belenger, Lab. de Chirurgie

Experimentale, 10, route des Jeunes, 1227 Geneva, Switzerland.

Oct. 23-25: 6th International Congress on Thrombosis. Monte Carlo. Organized by Mediterranean League Against Thromboembolic Diseases. Inquiries: Congress-Service. 1. rue Jules Lefebvre, 75009 Paris, France.

### AHA Scientific Sessions Future Meeting Dates

1980 — Miami Beach, Fl. — Nov. 17-20

1981 — Dallas, TX — Nov. 16-19

1982 — Dallas, TX - Nov. 15-18

1983 — Anaheim, CA - Nov. 14-17

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## N O T I C I A S

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### AMA NEWS:

#### *ANTIHISTAMINES EASE COLDS, RESEARCH PROJECT CONFIRMS*

Chicago — Antihistamines are effective in relieving the runny nose and congested sinuses of the common cold, says a research report in the Nov. 30 Journal of the American Medical Association.

Antihistamines have been widely used in non-prescription cold preparations for some years, but their value in relieving symptoms of the common cold had been the subject of considerable controversy. Some had contended the effect was mainly a placebo.

In the present study, 271 individuals with colds were studied. Some were given antihistamines (chlorpheniramine maleate) and others were given placebo. The antihistamines proved much superior to the placebo in lessening the degree of symptoms of the common cold, says J. Campbell Howard, MD, of Kenilworth, N. U. Differences were found on the first day and as late as the seventh day of the cold.

A side effect of drowsiness was noted among those taking antihistamines. This already had been known, and doctors have advised patients taking the product to avoid driving autos.

The antihistamines do not cure the cold, but merely make life somewhat more bearable while the illness is running its course.

to the hospital, says a report in the Nov. 30 Journal of the American Medical Association.

Emergency medical care systems have developed rapidly all over the nation in the last few years. Emphasis has been on quick stabilization of the patient and safe transportation to the hospital. Relief of pain has had low priority. Pain often helps in diagnosis and a strong pain-killer that masks symptoms would make it difficult to know where the patient hurts.

Researchers from the University of Texas Health Sciences Center at Dallas and the Dallas Fire Department experimented with a mixture of half nitrous oxide and half oxygen to relieve pain of accident victims and sufferers from heart attacks and other acute medical emergencies. The patients themselves were permitted to adjust the amount of inhalation of the substances, as needed to alleviate pain.

Of the 47 patients tested, 93 per cent experienced either partial or complete relief of pain. The effect of the gas wears off so quickly that the patients were conscious on reaching the hospital.

Nitrous oxide is useful as an analgesic in many types of injuries and illnesses. The paramedics administer it in consultation by two-way radio with the doctor at the emergency unit in the hospital. It is not used for individuals with head injuries, chest injuries, facial injuries and certain other conditions.

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#### *EMERGENCY VICTIMS EASE OWN PAIN WITH NITROUS OXIDE*

Chicago — Nitrous oxide to relieve pain has proved effective in accident victims and medical emergencies while the paramedics are rushing the patient

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#### *HEALTH AND MEDICAL EVENTS IN 1979 - A REVIEW BY THE AMERICAN MEDICAL ASSOCIATION*

Chicago — Americans ran for their lives in 1979. And they played tennis. And racquetball. And swam many laps in the pool. And roller skated.

The 1970s trend toward regular exercise and



better physical fitness peaked in the final year of the decade. Tens of millions of Americans were exercising more or less vigorously and more or less regularly. This definitely did more good than harm.

Along with exercise more and more Americans were doing better with other personal health habits. They were giving up cigarettes in such numbers that the nonsmokers predominate in most gatherings, and are much more likely to demand that the smokers refrain in the presence of others. Additional research studies further confirmed the health hazards of tobacco.

The U. S. has accomplished a "near revolution" in controlling high blood pressure, a top federal research chief declared at midyear. Widespread efforts to find persons with high blood pressure and get them in for treatment are paying off. Deaths from heart disease and stroke are dropping steadily year after year.

A survey of physicians by the American Medical Association early in 1979 revealed that Americans can be persuaded to change habits that are injurious to their health. In fact, many already are doing so on the urging of their doctors.

It is easier to lose weight or cut down on drinking than to give up smoking, the doctors found.

"Thou shalt not kill thyself" was the admonition to budding joggers in mid-year. Exercise is good for you, but, first, stop smoking, get your blood pressure under control, start a diet to lose two excess pounds. And start by walking, not running. Build up conditioning gradually.

For a few jogging can be fatal. Deaths during exercise are rare, but they do happen. One study told of 18 individuals who dropped dead during or shortly after jogging. For most of them there was no warning. They were seasoned, veteran runners who had no previous heart trouble.

As thousands of individuals competed in marathon races across the country, doctors warned that the races should be scheduled on cool days, and should start and finish in the morning, before the day heats up. Frequent gulps of water during the long races are needed to replace lost body fluids.

One researcher found that sprinters and distance runners have different types of muscle fibers in their legs. Thus, there are physical limits to the abilities of each runner, according to his genetic makeup.

Exercise is good for you, but lack of exercise increases a man's risk of heart disease very little, ano-

ther research team found. The other risk factors, cigarette smoking, overweight, high blood pressure, are more important than lack of exercise in boosting heart disease risk.

In organized sports, research continued to try to minimize risk of injury. One study found that deaths from organized football have declined markedly in recent years, but there has been an increase in broken necks resulting in complete paralysis. The National Football Head and Neck Injury Registry declared that the helmet-facemask system protects the head so well that players use it as a battering ram in tackling and blocking, thus causing more broken necks.

On another front, dialogue continued during 1979 regarding federal regulation of medical research and medical practice. Former HEW Assistant Secretary for Health, Charles C. Edwards, MD, charged in the fall of the year that "Wholesale federal regulation of the American health care system would fail to solve its economic problems and would be the most destructive, repressive, and reactionary step ever taken in the name of advancing the health of the people of this country." Several national health insurance proposals were before the Congress.

One example of federal regulation cited as having adverse effect was the continuous stream of announcements that many things found in the environment and the diet might cause cancer.

Giving animals huge doses of drugs to determine whether the drugs cause cancer does *not* tell scientists whether the drug would cause cancer in humans, one expert said. Another struck back at proposals to ban a commonly used pain killer simply because it is sometimes used in suicide attempts. And government agencies were accused of sometimes going off half cocked in labeling foods and drugs as cancer causing. Allegations against artificial sweeteners, food colorings and preservatives, pharmaceutical products, and industrial chemicals often are made on the basis of highly dubious and improperly conducted studies, said the editor of the Journal of the AMA.

An integral part of preventive medicine is cleaning up health hazards in the environment, and one study in Texas found that cleaner air positively does improve the health of those near the factory. Lead levels in children in a smelter area in El Paso dropped markedly after the smelter cleaned up its stack emissions. Another report from Colorado, showed clearly that air pollution can kill.

Genetics research caused considerable medical interest during the year, much of it highly speculative. The grim vision of the fictional 1984 probably will never happen, said one medical geneticist. Man-primate hybrids, cloning of human beings, and the production of men and women to genetic specifications are still far-fetched projections.

Genuine genetic insights, such as the DNA model, are confused with spectacular technological feats, like the "test tube baby." The DNA model is changing the way we view life, while the test tube baby is unlikely to alter the commonly used means of procreation, said one expert.

On the medical education front, a few individuals were saying that there already may be too many doctors. Most experts, however, pointed to waiting time for appointments and to some urban and rural neighborhoods still underserved medically. The AMA's Council on Medical Education conducted its 75th annual congress on medical education in Washington, with an international theme and top medical educators from throughout the world in attendance.

Some of the medical events of the year, as reported in the *Journal of the AMA* and many other scientific publications, were —

\* Heart disease continued to be the No. 1 killer of Americans. Research findings of bits and pieces of new knowledge surfaced during the year. One study found that moderate drinking - a beer or two, a glass or two of wine, a highball or two — actually reduced the risk of coronary death. Others promptly urged alcoholics not to use these results as an excuse to keep drinking.

\* Doctors were alerted during the year to watch for cases of a drug-resistant strain of malaria from Africa that has now reached the United States. The new malaria does not respond to the standard anti-malaria drugs.

\* The standard treatment used for the past 30 years for Hodgkin's Disease, a cancer of the lymph glands, works well against the disease, but also destroys sexual function, doctors found. It is possible to avoid this result by giving hormones along with the drug treatment.

\* Doctors were alerted to watch for a new form

of ringworm that does not show up under florescent light, the traditional diagnostic tool for the common scalp infection. The new ringworm responds to treatment, but diagnosis is difficult.

\* Smoking cigarettes was ruled out completely for women using "The Pill". Risk of vascular disease in women is sharply increased for smokers who use the popular oral contraceptive, one research team found.

\* Medical authorities throughout the nation continued vaccinating children against measles, and the Surgeon General of the United States declared that it is now possible to wipe out measles by 1982.

\* Further complicating the doctor's task in treating infection, Michigan researchers found that there is a marked increase in episodes of serious infection that are caused by several different bacteria in the body at the same time. The doctors call this poly-microbial bacteremia. Death rates are much higher among those with multiple infections.

\* New research studies confirmed effectiveness of a drug, tamoxifen citrate, or Nolvadex, in treating breast cancer that has spread to other parts of the body. Some individuals with advanced breast cancer that had failed to respond to other therapy showed improvement with Nolvadex treatment.

\* Regulations concerning the printed package insert explaining all about a drug were under discussion during the year. A New York state study found that most women still look first to their doctor to tell them about the drug, rather than merely reading about it in the insert.

\* An unusual injury — The Dnnk Laceration — appeared in the medical literature for the first time this year. It is a cut or bruise on the fingers or hand of the tall, agile basketball player who leaps high into the air and "dunks" the ball directly into the basket, instead of tossing it up from below. The injury comes when the hand strikes the rim of the basket on the way down.

## M E D I — Q U I Z

### VALVULA AORTICA

(Puede haber más de una contestación)

1. En válvulas aórticas estenóticas y calcificadas, cuál de los siguientes hallazgos físicos sugieren enfermedad valvular severa:
  - a. click ejetivo
  - b. segundo sonido cardíaco paradójicamente desdoblado
  - c. cuarto ruido cardíaco (pacientes menores de 45 años)
- 2.Cuál o cuáles de los siguientes hallazgos caracteriza a la insuficiencia aórtica aguda:
  - a. congestión pulmonar severa con un corazón dilatado
  - b. congestión pulmonar severa con un corazón de tamaño normal
  - c. cambios electrocardiográficos de ischemia
  - d. un electrocardiograma relativamente normal
3. En insuficiencia aórtica, cuál de los siguientes parametros indican un pobre pronóstico:
  - a. cardiomegalia en exceso de 60 por ciento del diámetro transtorácico
  - b. presión telediastólica mayor de 20 mm de Hg
  - c. cierre prematuro de la válvula mitral
  - d. todos los criterios mencionados
4. El soplo de la estenosis aórtica severa se caracteriza por lo siguiente:
  - a. intensidad máxima tarde en sistole, se ausculta en la base y se irradia hacia el cuello
  - b. disminuye en intensidad cuando existe el fallo congestivo severo
  - c. se ausculta frecuentemente en el apice o area xiphoidal en pacientes con emphysema pulmonar



5. Estenosis aórtica implica lo siguiente:
- a. el flujo anterogrado a través de la válvula no se puede aumentar significativamente no importa cuanto se aumente el gradiente de presión sistólica a través de la válvula
  - b. el área valvular aórtica es menor de  $.6 \text{ cm}^2$
  - c. Se puede encontrar con hipertensión arterial significativa en 6-10 por ciento de los casos
  - d. En estenosis aórtica crítica, se puede encontrar gradientes de presión sistólicos pequeños en presencia de débitos cardíacos bajos
6. Bloqueo atrio-ventricular completo en pacientes con endocarditis de la válvula aórtica indica:
- a. embolia coronaria
  - b. alrededor del anillo y en el tabique inter ventricular
  - c. rotura hacia el pericardio
7. El organismo más frecuente responsable por endocarditis infecciosa de la válvula aórtica es:
- a. *Strep viridans*
  - b. *Diplococo pneumonia*
  - c. *Staph aureus*
8. Endocarditis bacteriana afecta más frecuentemente cuál de las siguientes válvulas:
- a. aórtica
  - b. mitral
  - c. ambas
9. Las siguientes oraciones son ciertas excepto:
- a. La splenomegalia es común en endocarditis de la válvula tricuspídea sin involucramiento de la mitral o válvula aórtica

- b. Pacientes con estafilococcemia pueden desarrollar endocarditis en válvulas normales
- c. La bacteremia de endocarditis es esporádica

10. La lesión congénita que más frecuente se encuentra es:

- a. defectos inter-atriales
- b. defectos inter ventriculares
- c. válvula aórtica bicuspide

(Contestaciones en página 473)



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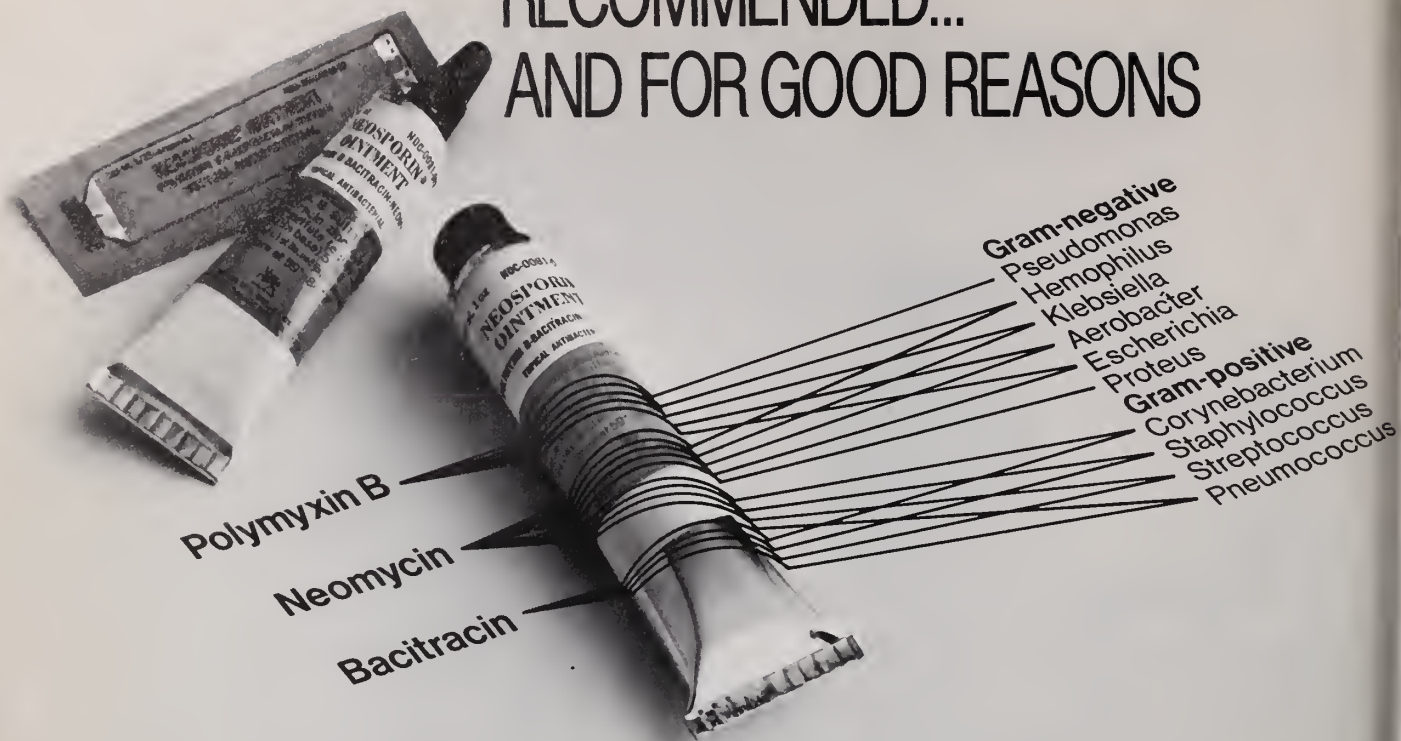
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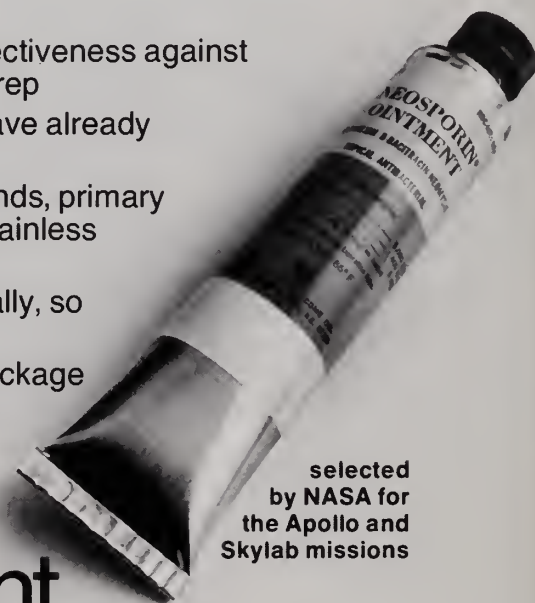
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**WARNING:** Because of the potential hazard of nephrotoxicity and ototoxicity due to neomycin, care should be exercised when using this product in treating extensive burns, trophic ulceration and other extensive conditions where absorption of neomycin is possible. In burns where more than 20 percent of the body surface is affected, especially if the patient has impaired renal function or is receiving other aminoglycoside antibiotics concurrently, not more than one application a day is recommended.

When using neomycin-containing products to control secondary infection in the chronic dermatoses, it should be borne in mind that the skin is more liable to become sensitized to many substances, including neomycin. The manifestation of sensitization to neomycin is usually a low grade reddening with swelling, dry scaling and itching; it may be manifest simply as a failure to heal. During long-term use of neomycin-containing products, periodic examination for such signs is advisable and the patient should be told to discontinue the product if they are observed. These symptoms regress quickly on withdrawing the medication. Neomycin-containing applications should be avoided for that patient thereafter.

**PRECAUTIONS:** As with other antibacterial preparations,

prolonged use may result in overgrowth of nonsusceptible organisms, including fungi. Appropriate measures should be taken if this occurs.

**ADVERSE REACTIONS:** Neomycin is a not uncommon cutaneous sensitizer. Articles in the current literature indicate an increase in the prevalence of persons allergic to neomycin. Ototoxicity and nephrotoxicity have been reported (see Warning section).

Complete literature available on request from Professional Services Dept. PML



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## AGRADECIMIENTO

*En este año a punto de terminar, la Junta Editora desea expresar su más profundo agradecimiento a todos los patrocinadores del Boletín de la AMPR, quienes con su apoyo, permiten nuestra labor y el logro de nuestros objetivos.*

*La Junta Editora desea expresar igualmente su agradecimiento a los siguientes compañeros médicos que durante el año que termina nos han brindado su desinteresada ayuda y colaboración en la evaluación de los artículos que se nos han sometido. La ayuda brindada por estos compañeros ha permitido una revista de actualidad que refleje la calidad de la medicina puertorriqueña.*

*Para todos, nuestro más profundo agradecimiento:*

Francisco Aguiló, MD  
José H. Amadeo, MD  
Juan M. Aranda, MD  
Guillermo Arbona, MD  
Robert Axtmayer, MD  
Natalio B. Bayonet, MD  
Ramón H. Bermúdez, MD  
Guillermo Blanco, MD  
Margarita Cáceres de Costas, MD  
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Luis Díaz Bonet, MD  
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Herman J.. Flax, MD  
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Edgardo Hernández López, MD  
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George H.. Hillyer, PhD  
Charles D. Johnson, MD  
Aldo E. Lanaro, MD  
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Hernán F. Méndez, MD  
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Adolfo Pérez Comas, MD  
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Guillermo Picó, MD  
Guillermo Picó, Jr. MD  
Enrique Piovanetti, MD  
Elí Ramírez, MD  
R. Ramírez González, MD  
Carlos H. Ramírez Ronda, MD  
Nathan Rifkinson, MD  
Julio V. Rivera, MD  
David Rodríguez, MD  
Eduardo A. Santiago Delpín, MD  
José E. Sifontes, MD  
Juan T. Tomasini, MD  
Víctor Torres, MD  
Marta I.. Valcárcel, MD  
Rafael Villavicencio, MD





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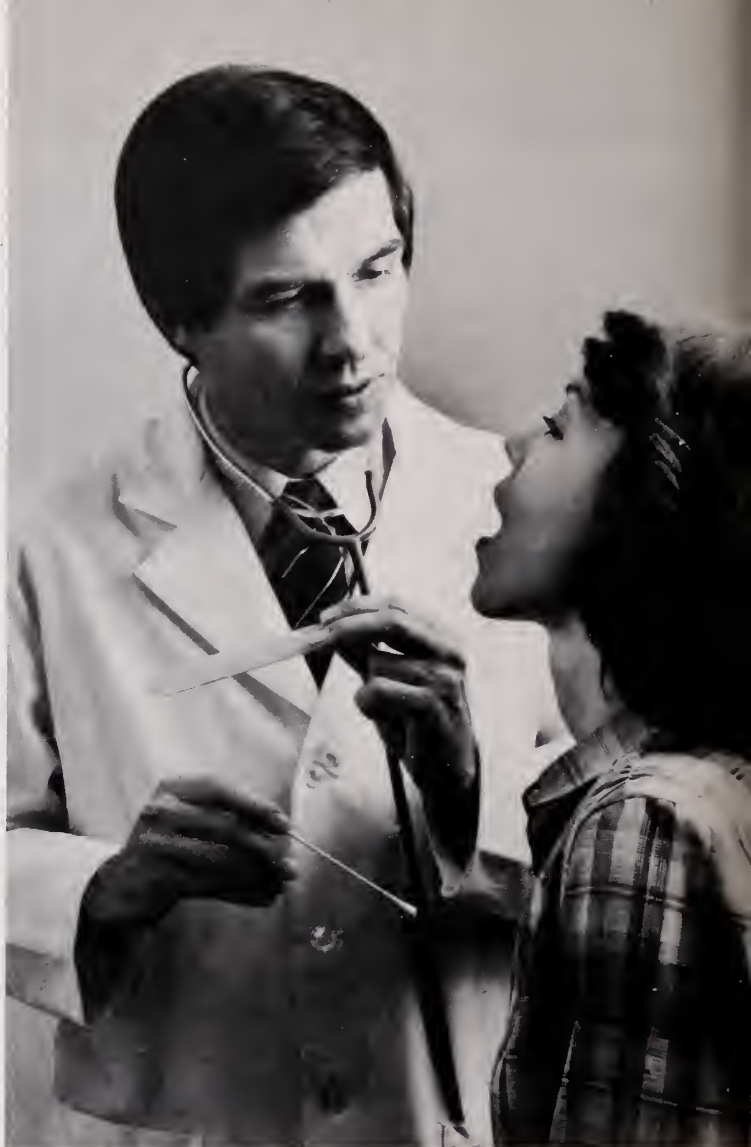
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Septra Suspension provides effective antibacterial action in urine and blood against susceptible strains of E coli, Klebsiella-Enterobacter and Proteus. Whether the infection centers in the kidneys or bladder, Septra Suspension maintains effective levels at the site of the infection with just two doses a day.

Adequate fluid intake should be maintained and frequent urinalyses with careful microscopic examination performed during Septra therapy. Septra is contraindicated in infants under two months of age.

\*In vitro data do not necessarily correlate with clinical results. Data on file, Burroughs Wellcome Co.

NOTE: Septra should not be used in the treatment of streptococcal pharyngitis.

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**INDICATIONS AND USAGE:**

**URINARY TRACT INFECTIONS:** For the treatment of urinary tract infections due to susceptible strains of the following organisms: *Escherichia coli*, *Klebsiella-Enterobacter*, *Proteus mirabilis*, *Proteus vulgaris*, *Proteus morgani*. It is recommended that initial episodes of uncomplicated urinary tract infections be treated with a single effective antibacterial agent rather than the combination.

**NOTE:** Currently, the increasing frequency of resistant organisms is a limitation of the usefulness of all antibacterial agents, especially in the treatment of these urinary tract infections.

**ACUTE OTITIS MEDIA:** For the treatment of acute otitis media in children due to susceptible strains of *Haemophilus influenzae* or *Streptococcus pneumoniae* when in the judgment of the physician Septra offers some advantage over the use of other antimicrobial agents. Limited clinical information is presently available on the effectiveness of treatment of otitis media with Septra when the infection is due to *Haemophilus influenzae* resistant to ampicillin. To date, there are limited data on the safety of repeated use of Septra in children under two years of age. Septra is not indicated for prophylactic or prolonged administration in otitis media at any age.

**SHIGELLOSIS:** For the treatment of enteritis caused by susceptible strains of *Shigella flexneri* and *Shigella sonnei* when antibacterial therapy is indicated.

**PNEUMOCYSTIS CARINII PNEUMONITIS:** For the treatment of documented *Pneumocystis carinii* pneumonitis. To date, this drug has been tested only in patients 9 months to 16 years of age who were immunosuppressed by cancer therapy.

**CONTRAINDICATIONS:** Hypersensitivity to trimethoprim or sulfonamides. Pregnancy and during the nursing period. Infants less than two months of age.

**WARNINGS: SEPTRA SHOULD NOT BE USED IN THE TREATMENT OF STREPTOCOCCAL PHARYNGITIS.**

Clinical studies have documented that patients with Group A  $\beta$ -hemolytic streptococcal tonsillopharyngitis have a greater incidence of bacteriologic failure when treated with Septra than do those patients treated with penicillin as evidenced by failure to eradicate this organism from the tonsillopharyngeal area.

Deaths associated with administration of sulfonamides have been reported from hypersensitivity reactions, agranulocytosis, aplastic anemia and other blood dyscrasias. Experience with trimethoprim alone is much more limited, but occasional interference with hematopoiesis has been reported as well as an increased incidence of thrombopenia with purpura in elderly patients on certain diuretics, primarily thiazides.

Sore throat, fever, pallor, purpura or jaundice may be early signs of serious blood disorders. Frequent CBCs are recommended; therapy should be discontinued if a significant reduction in the count of any formed blood element is noted.

**PRECAUTIONS:** Use with caution in patients with impaired renal or hepatic function, possible folate deficiency, severe allergy or bronchial asthma. In glucose-6-phosphate dehydrogenase-deficient individuals, hemolysis may occur (frequently dose-related). During therapy, maintain adequate fluid intake and perform frequent urinalyses with careful microscopic examination and renal function tests, particularly where there is impaired renal function.

Since Septra may prolong prothrombin time in patients on warfarin, coagulation time should be reassessed when Septra is given.

**ADVERSE REACTIONS:** All major reactions to sulfonamides and trimethoprim are included, even if not reported with Septra. **Blood Dyscrasias:** Agranulocytosis, aplastic anemia, megaloblastic anemia, thrombopenia, leukopenia, hemolytic anemia, purpura, hypoprothrombinemia and methemoglobinemia. **Allergic Reactions:** Erythema multiforme, Stevens-Johnson

syndrome, generalized skin eruptions, epidermal necrolysis, urticaria, serum sickness, pruritus, exfoliative dermatitis, anaphylactoid reactions, periorbital edema, conjunctival and scleral injection, photosensitization, arthralgia and allergic myocarditis. **Gastrointestinal Reactions:** Glossitis, stomatitis, nausea, emesis, abdominal pains, hepatitis, diarrhea and pancreatitis. **C.N.S. Reactions:** Headache, peripheral neuritis, mental depression, convulsions, ataxia, hallucinations, tinnitus, vertigo, insomnia, apathy, fatigue, muscle weakness and nervousness. **Miscellaneous Reactions:** Drug fever, chills, and toxic nephrosis with oliguria and anuria. Periarteritis nodosa and L. E. phenomenon have occurred.

Due to certain chemical similarities to some goitrogens, diuretics (acetazolamide and the thiazides) and oral hypoglycemic agents, sulfonamides have caused rare instances of goiter production, diuresis and hypoglycemia; cross-sensitivity may exist with these agents. In rats, long-term administration of sulfonamides has produced thyroid malignancies.

**DOSAGE AND ADMINISTRATION: Not recommended for use in infants less than two months of age.**

**URINARY TRACT INFECTIONS AND SHIGELLOSIS IN ADULTS AND CHILDREN AND ACUTE OTITIS MEDIA IN CHILDREN:**

**Adults:** The usual adult dosage for the treatment of urinary tract infections is two tablets or four teaspoonfuls (20 ml) every 12 hours for 10 to 14 days. An identical daily dosage is used for 5 days in the treatment of shigellosis.

**Children:** The recommended dose for children with urinary tract infections or acute otitis media is 8 mg/kg trimethoprim and 40 mg/kg sulfamethoxazole per 24 hours, given in two divided doses every 12 hours for 10 days. An identical daily dosage is used for 5 days in the treatment of shigellosis. The following table is a guideline for the attainment of this dosage using Septra Tablets or Suspension.

Children: Two months of age or older:

Weight		Dose—every 12 hours	
lb	kg	Teaspoonfuls	Tablets
22	10	1 ( 5 ml)	½
44	20	2 (10 ml)	1
66	30	3 (15 ml)	1½
88	40	4 (20 ml)	2 (or 1 DS tablet)

For patients with renal impairment:

Creatinine Clearance (ml/min)	Recommended Dosage Regimen
Above 30	Usual Standard Regimen
15-30	Half of the usual dosage regimen
Below 15	Use Not Recommended

**PNEUMOCYSTIS CARINII PNEUMONITIS:**

The recommended dosage for patients with documented *Pneumocystis carinii* pneumonitis is 20 mg/kg trimethoprim and 100 mg/kg sulfamethoxazole per 24 hours given in equally divided doses every 6 hours for 14 days. The following table is a guideline for the attainment of this dosage in children.

Weight		Dose—every 6 hours	
lb	kg	Teaspoonfuls	Tablets
18	8	1 ( 5 ml)	½
35	16	2 (10 ml)	1
53	24	3 (15 ml)	1½
70	32	4 (20 ml)	2 (or 1 DS tablet)

**HOW SUPPLIED:** TABLETS, containing 80 mg trimethoprim and 400 mg sulfamethoxazole—bottles of 40, 100, 500 and 1000 tablets; unit dose pack of 100.

**ORAL SUSPENSION,** containing the equivalent of 40 mg trimethoprim and 200 mg sulfamethoxazole in each teaspoonful (5 ml), cherry flavored—bottle of 450 ml. Also available in double strength, oval-shaped, pink, scored tablets containing 160 mg trimethoprim and 800 mg sulfamethoxazole—Compliance™ Pak of 20, bottle of 60 and unit dose pack of 100.



**Burroughs Wellcome Co.**  
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